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# A HISTOLOGICAL AND BIOCHEMICAL STUDY OF PATHOLOGICAL THYROID MATERIAL, WITH SPECIAL REFERENCE TO THE EFFECT OF LUGOL'S SOLUTION*

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THE investigation here reported has been carried out during the past three years with a view to throwing additional light upon: (1) the variation in the iodine content of pathological thyroid material, contrasted with the variation in the histological structure; (2) the effect of the administration of iodine upon the histological appearance, and upon the iodine content of pathological thyroid material. In the course of this investigation certain other chemical data were ascertained and recorded, although few conclusions can be drawn from them.

This paper will show in the following order:

A. The source of the material, and the initial treatment of it.

B. The clinical classification adopted, with a discussion of the classification used by other workers. (The clinical diagnosis for each case in our series was reached by taking into consideration the pre-operative diagnosis of the physician, together with a careful checking of the patient's history and an analysis of any laboratory examinations.)

C. The histological procedure employed, and the histological classification of the material.

D. The chemical procedure.

E. The results obtained, classified according to the clinical condition of the patient.

F. A discussion of these results and comparison with similar work as given in the literature.

## THE SOURCE OF THE MATERIAL, AND THE INITIAL TREATMENT OF IT

In all 126 thyroids were obtained, two at post-mortem and the remainder from the operating rooms of the Winnipeg General Hospital. I am indebted to Drs. B. J. Brandson, N. J. Maclean, J. E. Lehmann, and other members of the attending staff. I am especially indebted to Dr. G. S. Fahrni because of the number of cases he has permitted me to use.

The material was obtained at operation, and immediately separated into two portions. The first was cut into blocks, as will be described in a later paragraph, and fixed in 5 per cent formalin. The other portion was weighed and placed in a drying oven. It was considered essential that only the freshest of material should be used. In each case the gland was in the fixing solution or drying oven within thirty minutes of its removal from the patient.

## CLINICAL CLASSIFICATION

The classification of this thyroid material from a clinical standpoint has presented considerable difficulty. The surgeon in attendance on each case had, of course, made a pre-operative diagnosis. His distinction was always clear cut and accurate between the toxic and the non-toxic glands, but sufficient differentiation was not always made between the different

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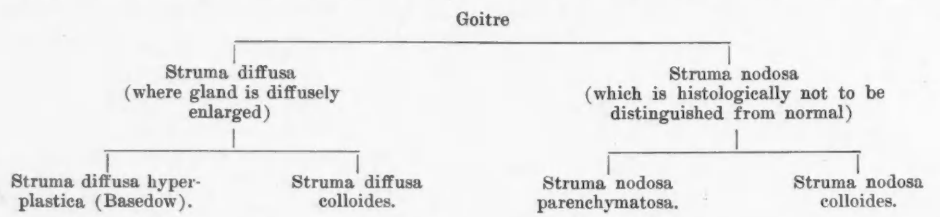
varieties of the toxic group, *e.g.*, some cases were diagnosed as Graves' disease which showed rather mild toxic symptoms. It was therefore necessary to check carefully each history, with especial reference to recorded symptoms, the metabolic rate, the response of the pulse rate to Lugol's solution, the blood pressure, etc.

The thyroid material has been divided clinically into *normal, colloid, adenoma, toxic adenoma,* and *the thyroid of Graves' disease.* It will be seen here that an attempt has been made towards simplicity, although some writers would even shorten this list, their contention being that Graves' disease and the hyperthyroidism of toxic adenoma are esentially the same disease. I believe the differentiation of these two diseases, as enunciated by Plummer, to be correct. "Whereas exophthalmic goitre is a disease of rapid onset averaging nine months' duration, and occurring most frequently in young persons, toxic adenoma is a chronic condition averaging four years in onset and occurring, as a rule, in persons more than forty years of age. In exophthalmic goitre the symptoms of hyperthyroidism progress by a series of waves, at the crest of which all the symptoms are exaggerated and a crisis occurs. In toxic adenoma the hyperthyroidism progresses insidiously and slowly, causing a permanent damage to the heart, kidneys, and other organs. . . . Hyperthyroidism occurs in this type of goitre (toxic adenoma) with a proportionately high diastolic pressure, in contrast to a slightly elevated systolic and a low diastolic pressure in exophthalmic goitre. In adenomatous goitre not only is there a slow development of toxic symptoms but there is usually a history of goitre of sixteen years' duration or more." The confusion of thyroid nomenclature is stressed by Boyd[1] when he states: "In man many different forms of goitre have been described, and we have such names as colloid goitre, parenchymatous goitre hyperplastic goitre, adenomatous goitre, toxic and non-toxic adenoma, cystic goitre, exophthalmic goitre, diffuse adenomatosis of the thyroid, etc. It is very desirable to decide, if possible, whether these are different diseases, or merely varying manifestations of the same process."

In 1863 Virchow[2] said: "With reference to true goitre the opinion has long been held that it comprises a series of definite varieties (struma lymphatica, cystica, ossea, vasculosa, etc.) which can develop independently of each other. This is wrong. All these so-called varieties are only different methods of development of essentially the same form of goitre." Although the tendency to-day is to revert to Virchow's expressed opinion, Plummer, as quoted above, apparently has ample grounds for making a differentiation between Graves' disease and toxic adenoma.

The following classification (Wegelin)[3] seems to be generally accepted in Germany.


Goitre
Struma diffusa (where gland is diffusely enlarged)
Struma nodosa (which is histologically not to be distinguished from normal)
Struma diffusa hyperplastica (Basedow).
Struma diffusa colloides.
Struma nodosa parenchymatosa.
Struma nodosa colloides.

### HISTOLOGICAL PROCEDURE EMPLOYED AND HISTOLOGICAL CLASSIFICATION

An effort was always made to obtain for histological study a cross section of the gland. A block of fresh tissue was cut approximately 2 inches by ½ by ½ in size. This was divided into three portions as shown in Fig. 1. These blocks remained attached to each other by a small area. The blocks were not completely separated until after being embedded in paraffin and prepared for sectioning.

Each block of tissue was cut in three ways as shown in Fig. 2. It was hoped that by this method of embedding and sectioning an accurate idea of the structure of the gland would be obtained. The sections were cut 0.7 $\mu$ in thickness and stained with hæmatoxylin and eosin. In the majority of cases four blocks of tissue were used: 463 blocks in all were made.

From a study of a large number of mammalian thyroids (cattle, sheep, dogs, etc.) Marine and Lenhart[4] came to the conclusion that there are

three fundamental types; (a) normal, (b) actively hyperplastic, and (c) colloid. There is difficulty in fitting all human thyroids into these three primary types. My observations are in full agreement with the view of many previous workers that a pure gland is unknown in human thyroid material, except in the active hyperplasias of childhood, puberty and pregnancy. Boyd[5] expresses very well the difficulties of classification when he writes:

"The more one sees of goitre, the less is one inclined to subdivide the lesions too minutely. If the reader will take a series of cases and study a number of blocks from each thyroid he will be surprised to find how varied are the lesions in any one gland. A simple or colloid goitre is supposed to be one in which the gland is in a completely resting condition, and yet evidence of hyperplasia can nearly always be found if it is looked for. Exophthalmic goitre is characterized by a general hyperplasia; but colloid areas indicating involution are found in all but the most fulminating cases. Finally, adenomata when well developed form a striking gross feature, but more or less complete localization and encapsulation of areas can be found in glands in which the enlargement to the naked eye appears to be quite diffuse. It is not too much to say that quite often in a single section we can see areas characteristic of exophthalmic goitre, of colloid goitre, and of adenomatous goitre. The differences are quantitative rather than qualitative."

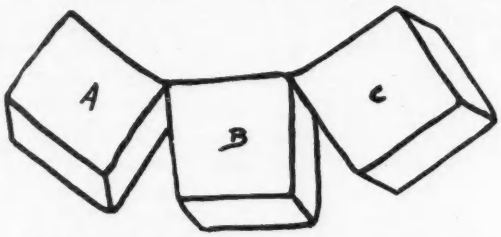



FIG. 1.—Histological study; preparation of tissue for fixing and embedding.

It was also pointed out by Hale White[6] that if one examined any large series of human thyroids he would find great variations in histological appearance in subjects which during life showed no manifestations of diseases known to be associated with thyroid changes.

Bearing in mind these difficulties, and recognizing the fact that the tendency is for the glands to be of a mixed type, the proportion of the component varieties being subject to wide variations, the author has classified the gland histologically into (1) normal, (2) colloid, (3) fetal adenoma, (4) (non-toxic) adenoma, (5) toxic adenoma, and (6) the gland present in Graves' disease. One case of malignant thyroid was found in my series, see Fig. 10.

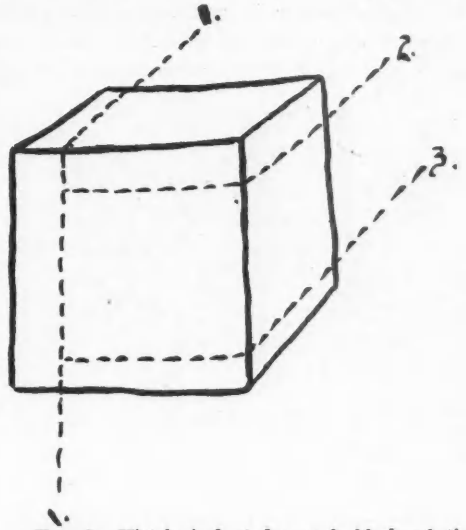



FIG. 2.—Histological study; each block of tissue was cut in the three different planes.

*Normal gland.*—Microscopically the normal gland is seen to consist of follicles which are generally round or oval in shape. These are

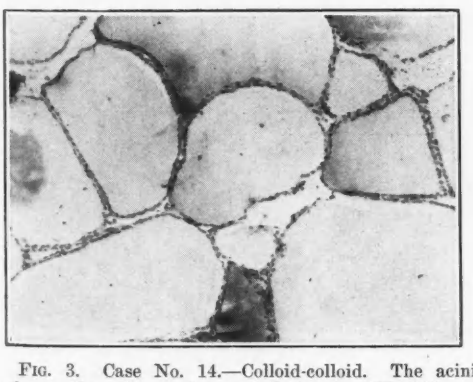


FIG. 3. Case No. 14.—Colloid-colloid. The acini are large, the cells are low and flattened. (X 100).

FIG. 4. Case No. 52.—Adenoma-colloid. Involuted adenoma; there is no hyperplasia and many phagocytic cells are seen in the large acinus. (X 100).

closed spaces of somewhat irregular size. They are lined with a single layer of flat cubical, or, at the most, cubical epithelium. The cells are quite regular in size. The nuclei are small, basal, darkly-staining, and vesicular. The colloid material lies in contact with the free border of the epithelial cells. It is homogeneous and stains deeply with eosin.

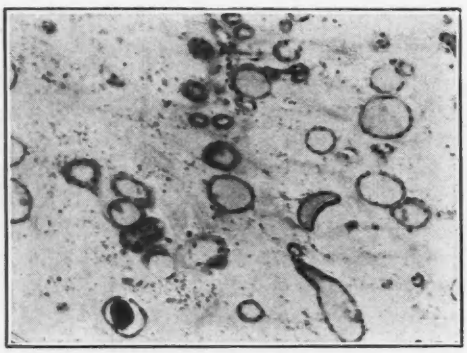


FIG. 5. Case No. 20.—Fetal adenoma. (X 100).

FIG. 6. Case No. 11.—Toxic adenoma-adenoma. There is some epithelial hyperplasia and well marked lymphoid hyperplasia. (X 100).

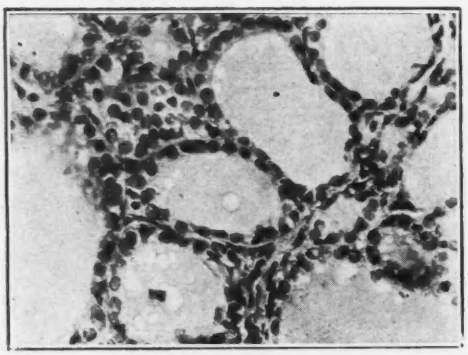


FIG. 7. Case No. 27.—Graves' toxic adenoma. The gland is involuting. Note the vacuolated appearance of the colloid. (X 300).

*Colloid gland.*—Microscopically the colloid gland seems at first to resemble normal tissue, but more careful examination shows evidence of involution and former hyperplasia, and many of the acini are greatly dilated so that the lining epithelium is correspondingly flattened. The acini are filled with densely stained colloid. Other acini are much smaller than normal. Traces of former hyperplasia can be seen in the form of spurs of epithelium which project into the lumina of the acini. Islands of still active hyperplasia may be found if the search is sufficiently careful.

*Fetal adenoma.*—In fetal adenoma the acini are widely separated by a peculiar material, the exact nature of which is difficult to determine. In most places it is hyaline and structureless and may so resemble the colloid within the acini in its staining characteristics that it appears as if the colloid had flowed out into the inter-acinar spaces. More frequently, however,

FIG. 8. Case No. 42.—Graves-adenoma. Graves' showing involution. The branched process resembling an intestinal villus is well seen. Epithelial cell—low columnar. (X 100).

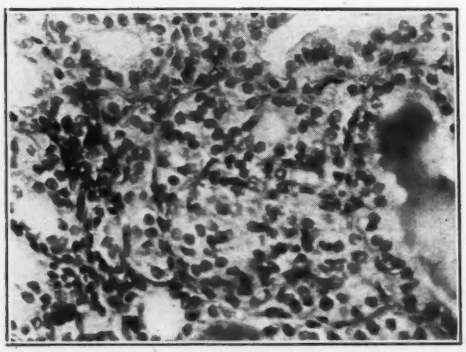


FIG. 9. Case No. 44.—Graves-Graves. There is very active hyperplasia. It is almost a solid cellular mass. The tall columnar cell is well seen. (X 300).

this homogeneous substance stains more faintly than the colloid.

*Adenoma. Toxic adenoma. The thyroid of Graves' disease.* — It is recognized that these terms, current in the literature, are not satisfactory, but they indicate a distinction recognized by many authors and which the present study seems to support. The writer believes that our conception of these conditions will be simplified if they are regarded as a matter of degree—the degree of hyperplasia. It can be definitely stated that the toxicity of the gland is directly proportional to the number and to the extent of the hyperplastic areas.

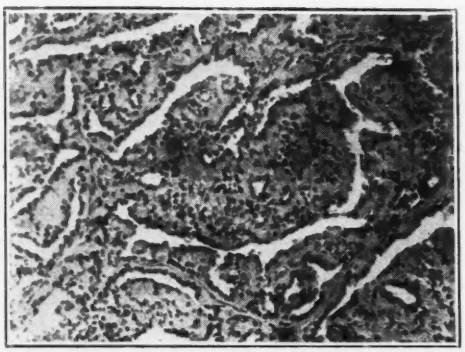


FIG. 10. Case No. 84.—Malignant thyroid; papillary adenoma. In places the papillæ are regular and covered by a single layer of syncytial cuboidal cells. The acini are very irregular and hyperchromatism is marked. (X 100).

## CHEMICAL PROCEDURES EMPLOYED

*Water percentage of the whole gland.*—The fresh gland was weighed and then dried in an oven at 105° C. until a constant weight was obtained. This procedure usually required from seventy-two to ninety-six hours.

*Fat percentage of the dehydrated gland.*—The fat was extracted with ether for twelve hours in a Soxhlet apparatus. The ether was evaporated off, and the residue of fat weighed.

*Nitrogen percentage of dehydrated gland*—Total nitrogen estimation was done according to Kjeldahl's procedure on 0.200 gms. of material. Estimations were made in groups of four, and duplicate estimations were done on one of every four. The results were discarded if the percentage of difference in the duplicates was greater than 0.5 and the whole group repeated.

*Iodine percentage of the dried gland.*—The iodine percentage was obtained by Kendall's[7] method, using 0.4 gms. of material. In the tables the results are expressed for dry, fat free, and for fresh material. Duplicate estimations were performed on every third case. Blanks were also run for each set of estimations. A trace of iodine in the blank caused the discarding of that group of results, and where there was a difference in duplicates greater than 0.5 per cent the analysis was repeated for that group.

## RESULTS

The cases are divided into those which had received and those which had not received iodine medication. It must, however, be emphasized that it is extremely difficult to be certain that a patient has received no iodine medication whatever. Another factor which must be borne in mind in this country is the extensive use of iodized salt. This is stated to be 1 part of potassium iodide in 10,000, a content twenty-five times greater than is deemed necessary by authorities in such a goitrous country as Switzerland. The results of all cases receiving iodine medication are summarized in Table I. The results of all cases receiving no iodine medication are summarized in Table II.

The cases have been divided into groups according to the clinical diagnosis (ref. Sect. B.) and according to the histological findings (ref. Sect. C.).

The iodine results in detail for each case, together with the metabolic rates and the amount of iodine administered are given in Tables III and IV. A copy of the detailed results showing water percentage of the whole gland, the fat percentage of the dehydrated gland and the nitrogen percentage of the dried gland has been filed in the Medical College Library, University of Manitoba, for record.

## DISCUSSION OF RESULTS AND COMPARISON WITH SIMILAR WORK GIVEN IN THE LITERATURE

*Water percentage of whole gland.*—The average varies in the different groups from 82.5 to 75.8 per cent. The highest value obtained for any single case being 93.3, and the lowest, 65.9 per cent.

*Fat percentage of dehydrated gland.*—The average value for the different groups varies from 3.50 to 0.51 per cent, the highest value

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obtained for any single case being 5.7 and the lowest 0.07 per cent.

*Nitrogen content of dried gland.*—The average value for the different groups varies from 14.2 to 10.6 per cent, the highest value obtained for any single case being 15.5 and the lowest 10.1 per cent.

*Iodine percentage of dried gland.*—The average percentage for the different groups varies from 0.445 to 0.012 per cent, the highest value obtained for any single case being 0.549, the lowest 0.012 per cent.

*Iodine percentage in fresh gland.*—The average iodine percentage in fresh gland varies from 0.1031 to 0.0021 per cent, the highest value obtained for any single case being 0.1149 and the lowest 0.0021 per cent.

TABLE I.

Iodine Given

| Group No. | Clinical diagnosis | Histolog. diagnosis | No. Cases | Water per cent of whole gland | | | Fat per cent of dehydrated gland | | | Nitrogen per cent dried gland | | | Iodine per cent in dried gland | | | Iodine per cent in fresh gland | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Max. | Min. | Aver. | Max. | Min. | Aver. | Max. | Min. | Aver. | Max. | Min. | Aver. | Max. | Min. | Aver. |
| I. | Normal | No cases | | | | | | | | | | | | | | | | |
| II. | Colloid | Colloid | 2 | 79.9 | 72.3 | 76.1 | 3.04 | 1.25 | 2.15 | 12.3 | 11.7 | 12.0 | 0.463 | 0.428 | 0.445 | 0.1149 | 0.0913 | 0.1031 |
| III. | Adenoma | Colloid | 8 | 80.8 | 72.7 | 76.7 | 2.60 | 0.50 | 1.06 | 13.9 | 11.5 | 12.6 | 0.517 | 0.100 | 0.338 | 0.1130 | 0.0252 | 0.0763 |
| IV. | Toxic Adenoma | Colloid | 4 | 81.2 | 76.7 | 78.6 | 2.90 | 0.22 | 1.11 | 13.3 | 10.5 | 11.8 | 0.429 | 0.144 | 0.309 | 0.1044 | 0.0330 | 0.0696 |
| V. | Graves' | Colloid | 8 | 83.2 | 72.7 | 79.1 | 2.90 | 0.79 | 1.52 | 14.0 | 10.1 | 12.4 | 0.549 | 0.086 | 0.271 | 0.1094 | 0.0170 | 0.0576 |
| VI. | Fetal Adenoma | Fetal Adenoma | No cases | | | | | | | | | | | | | | | |
| VII. | Adenoma | Fetal Adenoma | 2 | 83.9 | 77.9 | 80.9 | 1.93 | 1.67 | 1.80 | | | 10.6 | 0.379 | 0.105 | 0.242 | 0.0824 | 0.0165 | 0.0494 |
| VIII. | Graves' | Fetal Adenoma | No cases | | | | | | | | | | | | | | | |
| IX. | Adenoma | Adenoma | 3 | 82.0 | 80.0 | 80.8 | 1.26 | 0.50 | 0.99 | 15.5 | 12.2 | 13.9 | 0.308 | 0.081 | 0.184 | 0.0547 | 0.0161 | 0.0343 |
| X. | Toxic Adenoma | Adenoma | 3 | 89.0 | 74.1 | 80.5 | 0.89 | 0.24 | 0.51 | 13.7 | 11.7 | 12.7 | 0.211 | 0.130 | 0.166 | 0.0334 | 0.0232 | 0.0296 |
| XI. | Graves' | Adenoma | 12 | 84.5 | 77.0 | 80.2 | 2.60 | 0.51 | 1.34 | 14.1 | 11.7 | 12.8 | 0.338 | 0.054 | 0.184 | 0.0746 | 0.0100 | 0.0359 |
| XII. | Toxic Adenoma | Toxic Adenoma | 6 | 84.4 | 75.6 | 80.8 | 4.10 | 0.59 | 2.06 | 14.6 | 11.7 | 13.2 | 0.254 | 0.0250 | 0.125 | 0.0609 | 0.0052 | 0.0227 |
| XIII. | Graves' | Toxic Adenoma | 9 | 93.3 | 79.5 | 82.5 | 2.90 | 0.07 | 1.39 | 14.5 | 11.1 | 12.4 | 0.382 | 0.068 | 0.227 | 0.0719 | 0.0104 | 0.0383 |
| XIV. | Graves' | Graves' | 10 | 83.2 | 79.8 | 81.2 | 5.70 | 0.38 | 1.76 | 14.8 | 10.1 | 12.3 | 0.382 | 0.186 | 0.209 | 0.0672 | 0.0190 | 0.0373 |
| XV. | Malignant | Thyroid | No cases | | | | | | | | | | | | | | | |

### A Detailed Study of the Iodine Results

*Cases receiving no iodine.*—The colloid group shows an average iodine content equal to the normal and this content varies within the normal range. The normal content is given by Cameron[8] as 0.2 to 0.086 per cent. Classes other than colloid show a value of 0.1 per cent, or less (dry tissue). Results found for colloid glands are higher than those reported elsewhere but this may be explained by the fact that in these "no-iodine" cases it is difficult to be sure that no iodine has been given. The lowest iodine value was found for a fetal adenoma.

*Cases receiving iodine.*—These show increased iodine values throughout all classes. The highest values are seen in pure colloid or in a gland which as a result of treatment has reverted to colloid. This difference is shown most clearly by a comparison of the value for fresh tissue, and this is naturally the case, since this actually expresses the concentration of iodine per unit volume.

*Effects of iodine.*—The thyroid gland, whatever its type, shows an increased iodine content after a course of Lugol's solution. All cases which under treatment present a colloid appearance stand apart as having a high iodine content. In those glands which show histologically a predominating colloid appearance there seems to be some relation between the iodine content and the amount of iodine given (ref. Table V.) This, however, cannot be stressed because of the difficulty of ascertaining the exact amount of iodine administered to the patient. This relationship does not hold for the gland whose histological appearance is that of an adenoma or Graves' disease.

The same iodine dosage does not appear to

have the same effect on the histology of different glands, assuming that the clinical condition can be regarded as an approximate index to the histological condition of the gland prior to treatment. The glands of the toxic group (toxic adenoma and Graves') which are untreated with iodine show a relatively low iodine content. The glands of the toxic group (toxic adenoma and Graves' disease) which are treated with iodine, and which after treatment retain histologically toxic characteristics, show an intermediate value.

It can be definitely stated that the iodine content of a toxic gland increases proportionately as the gland approximates to the colloid picture.

TABLE II.

No Iodine Given

| Group No. | Clinical diagnosis | Histolog. diagnosis | No. Cases | Water per cent of whole gland | | | Fat per cent of dehydrated gland | | | Nitrogen per cent dried gland | | | Iodine per cent in dried gland | | | Iodine per cent in fresh gland | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Max. | Min. | Aver. | Max. | Min. | Aver. | Max. | Min. | Aver. | Max. | Min. | Aver. | Max. | Min. | Aver. |
| I. | Normal | Thyroid | 2 | 83.1 | 80.0 | 81.5 | 2.60 | 1.20 | 1.90 | 14.0 | 12.8 | 13.4 | 0.306 | 0.105 | 0.206 | | | |
| II. | Colloid | Colloid | 3 | 80.5 | 79.8 | 80.2 | 4.50 | 0.37 | 2.03 | 12.5 | 12.2 | 12.3 | 0.453 | 0.232 | 0.355 | 0.0872 | 0.0443 | 0.0685 |
| III. | Adenoma | Colloid | 9 | 81.8 | 72.1 | 78.3 | 2.80 | 0.12 | 1.37 | 14.5 | 10.6 | 12.9 | 0.259 | 0.045 | 0.156 | 0.0513 | 0.0112 | 0.0320 |
| IV. | Toxic Adenoma | Colloid | No cases | | | | | | | | | | | | | | | |
| V. | Graves' | Colloid | No cases | | | | | | | | | | | | | | | |
| VI. | Fetal Adenoma | Fetal Adenoma | No cases | | | | | | | | | | | | | | | |
| VII. | Adenoma | Fetal Adenoma | 7 | 84.9 | 79.6 | 81.9 | 2.90 | 0.37 | 1.37 | 14.8 | 12.5 | 13.2 | 0.123 | 0.022 | 0.057 | 0.0211 | 0.0038 | 0.0101 |
| VIII. | Graves' | Fetal Adenoma | No cases | | | | | | | | | | | | | | | |
| IX. | Adenoma | Adenoma | 4 | 80.5 | 65.9 | 75.8 | 1.80 | 0.34 | 0.83 | 14.8 | 13.0 | 14.0 | 0.173 | 0.039 | 0.114 | 0.0370 | 0.0132 | 0.0250 |
| X. | Toxic Adenoma | Adenoma | 1 | | | 82.0 | | | 3.50 | | | 12.7 | | | 0.115 | | | 0.0198 |
| XI. | Graves' | Adenoma | 1 | | | 80.8 | | | 2.30 | | | 13.5 | | | 0.113 | | | 0.0211 |
| XII. | Toxic Adenoma | Toxic Adenoma | 1 | | | 80.4 | | | 4.20 | | | 14.2 | | | 0.012 | | | 0.0021 |
| XIII. | Graves' | Toxic Adenoma | No cases | | | | | | | | | | | | | | | |
| XIV. | Graves' | Graves' | No cases | | | | | | | | | | | | | | | |
| XV. | Malignant | Thyroid | 1 | | | 79.9 | | | 0.30 | | | 10.8 | | | 0.056 | | | 0.0110 |

## LITERATURE

Baumann[9] first showed in 1896 that the thyroid gland contains a large quantity of iodine. Thyroid physiology seems to have centred around this point since that time. The thyroid is the only organ in the body which has the power of storing iodine. The other tissues contain quantities of a much lower grade of magnitude.

The administration of iodine in the treatment of goitre goes back to Roger's seaweed prescription in the twelfth century. In 1863, Trousseau accidently gave tincture of iodine to a patient with Graves' disease, and noticed marked improvement. Iodide has been used extensively in Switzerland for the prevention of endemic goitre.

Many studies have been made of the iodine content of goitre. A table of historical value is given by Lunde, Closs and Wülfert.[10] Pioneers in the field, working with less accurate methods of iodine estimation, were Baumann,[9] Oswald,[11] Marine and Lenhart.[12]

Chief interest has centred recently around the effect of iodine on hyperthyroidism. Many papers on this subject have been presented. Of special importance is the work of Boothby,[13] Carson and Dock,[14] Fraser,[15] Hellwig,[16] Marine,[17] Marine and Lenhart,[4] Neisser,[18] Starr *et al*,[19] and Van Dyke.[20] In 1922 Cameron[8] made a complete review of the biochemistry of the gland, as known to that date. (See also *Canad. M. Ass. J.*, this issue p. 231).

Webster[21] has recently published a study of the reaction of simple goitre to iodine in which the histological findings are stressed.

Combined histological and biochemical studies in Graves' disease have been carried on by Kocher,[22] Cattell,[23] Marine,[24] and Reinhoff.[25]

Conjoint histological and biochemical study of all types of pathological thyroid material

TABLE III.

| Individual Results | | | Iodine Administered | | |
|---|---|---|---|---|---|
| Group No. | Case No. | B. M. R. | Iodine Medication Lugol's Sol. | Iodine Fresh Gland | Content Dried Gland |
| | | per cent | minims | per cent | per cent |
| II. | 65 | + 6 | 120 | 0.428 | 0.1149 |
| | 102 | +15 | 140 | *0.463 | 0.0913 |
| III. | 10 | +30 | 168 | *0.337 | 0.0798 |
| | 47 | + 9 | 80 | 0.386 | 0.0888 |
| | 61 | +27 | 140 | 0.354 | 0.0673 |
| | 66 | .. | large | *0.496 | 0.1125 |
| | 70 | +40 | 40 | *0.251 | 0.0677 |
| | 74 | +24 | 72 | *0.100 | 0.0252 |
| | 80 | +34 | 630 | 0.517 | 0.1130 |
| | 81 | +18 | 160 | 0.262 | 0.0562 |
| IV. | 30 | +36 | 60 | 0.144 | 0.0330 |
| | 67 | +40 | 80 | *0.354 | 0.1044 |
| | 82 | +45 | large | 0.309 | 0.0611 |
| | 121 | .. | 140 | *0.429 | 0.0799 |
| V. | 5 | .. | 120 | 0.273 | 0.0480 |
| | 22 | .. | 72 | 0.140 | 0.0325 |
| | 49 | .. | 60 | *0.086 | 0.0170 |
| | 53 | +52 | 140 | *0.363 | 0.0802 |
| | 73 | +42 | 220 | 0.249 | 0.0669 |
| | 86 | +42 | 180 | 0.261 | 0.0513 |
| | 90 | +48 | large | 0.338 | 0.0554 |
| | 97 | +55 | 140 | *0.549 | 0.1094 |
| VII. | 45 | +26 | 100 | 0.105 | 0.0165 |
| | 83 | +41 | 360 | 0.379 | 0.0824 |
| IX. | 34 | +11 | 700 | *0.308 | 0.0547 |
| | 63 | +16 | 140 | 0.081 | 0.0161 |
| | 91 | .. | 30 | *0.162 | 0.0320 |
| X. | 50 | +30 | large | 0.130 | 0.0334 |
| | 57 | +43 | 560 | *0.157 | 0.0323 |
| | 76 | +40 | 140 | 0.211 | 0.0232 |
| XI. | 9 | +50 | 160 | 0.273 | 0.0524 |
| | 25 | .. | 100 | *0.179 | 0.0400 |
| | 29 | +38 | 60 | 0.190 | 0.0303 |
| | 48 | +51 | 150 | *0.187 | 0.0374 |
| | 54 | +49 | 140 | 0.338 | 0.0746 |
| | 55 | +46 | 240 | 0.212 | 0.0419 |
| | 56 | +43 | 160 | *0.192 | 0.0291 |
| | 68 | +40 | 560 | 0.237 | 0.0447 |
| | 72 | .. | 100 | 0.152 | 0.0294 |
| | 75 | +32 | 80 | *0.110 | 0.0228 |
| | 77 | +42 | 150 | 0.092 | 0.0210 |
| | 100 | +51 | 240 | *0.054 | 0.0100 |
| XII. | 15 | +37 | 48 | 0.149 | 0.0222 |
| | 17 | +17 | 280 | *0.106 | 0.0169 |
| | 58 | +55 | 400 | 0.114 | 0.0208 |
| | 89 | .. | 150 | *0.254 | 0.0609 |
| | 103 | +47 | 80 | *0.025 | 0.0052 |
| | 105 | +57 | 240 | 0.101 | 0.0166 |
| XIII. | 19 | +57 | 240 | *0.206 | 0.0309 |
| | 24 | +43 | 240 | 0.321 | 0.0651 |
| | 27 | +75 | large | 0.280 | 0.0573 |
| | 31 | +27 | 315 | *0.382 | 0.0719 |
| | 37 | +45 | 200 | *0.068 | 0.0104 |
| | 42 | +71 | large | *0.309 | 0.0203 |
| | 79 | +68 | 280 | 0.152 | 0.0284 |
| | 85 | +47 | 180 | 0.239 | 0.0444 |
| | 99 | +46 | 50 | *0.086 | 0.0163 |
| XIV. | 8 | +56 | 140 | 0.211 | 0.0396 |
| | 13 | +70 | 480 | 0.280 | 0.0548 |
| | 40 | +32 | 100 | 0.107 | 0.0212 |
| | 41 | +40 | 540 | *0.304 | 0.0544 |
| | 44 | +45 | 280 | *0.382 | 0.0672 |
| | 64 | +60 | 140 | 0.155 | 0.0299 |
| | 69 | .. | 400 | 0.144 | 0.0285 |
| | 92 | +77 | 300 | *0.199 | 0.0328 |
| | 94 | +55 | 330 | 0.208 | 0.0349 |
| | 95 | +36 | 60 | 0.106 | 0.0190 |

*Duplicate Estimation.

TABLE IV.

| Individual Results | | | No Iodine Administered | | |
|---|---|---|---|---|---|
| Group No. | Case No. | B. M. R. | Iodine Medication Lugol's Sol. | Iodine Fresh Gland | Content Dried Gland |
| | | per cent | minims | per cent | per cent |
| I. | 1 | .. | .. | *0.105 | .. |
| | 2 | .. | .. | 0.306 | .. |
| II. | 14 | .. | .. | *0.232 | 0.0443 |
| | 46 | 3 | .. | *0.380 | 0.0741 |
| | 101 | 8 | .. | 0.453 | 0.0872 |
| III. | 4 | .. | .. | 0.168 | 0.0318 |
| | 26 | 17 | .. | *0.045 | 0.0112 |
| | 28 | 4 | .. | *0.108 | 0.0209 |
| | 35 | 20 | .. | 0.191 | 0.0345 |
| | 52 | .. | .. | *0.161 | 0.0420 |
| | 78 | 44 | .. | 0.106 | 0.0274 |
| | 88 | .. | .. | 0.249 | 0.0456 |
| | 93 | 15 | .. | *0.259 | 0.0513 |
| | 98 | 18 | .. | 0.119 | 0.0235 |
| VII. | 3 | .. | .. | *0.082 | 0.0128 |
| | 20 | .. | .. | 0.027 | 0.0053 |
| | 36 | 25 | .. | *0.123 | 0.0211 |
| | 39 | 3 | .. | *0.038 | 0.0074 |
| | 60 | 10 | .. | *0.038 | 0.0056 |
| | 71 | 34 | .. | 0.022 | 0.0038 |
| | 87 | .. | .. | 0.105 | 0.0207 |
| IX. | 16 | 25 | .. | *0.173 | 0.0370 |
| | 18 | 22 | .. | 0.073 | 0.0139 |
| | 23 | .. | .. | 0.170 | 0.0360 |
| | 32 | .. | .. | *0.039 | 0.0132 |
| X. | 11 | 42 | .. | 0.115 | 0.0198 |
| XI. | 7 | .. | .. | 0.113 | 0.0211 |
| XII. | 6 | 40 | .. | *0.012 | 0.0021 |
| | 84 | 19 | .. | 0.056 | 0.0111 |

*Duplicate Estimation.

does not appear to have been carried out on this continent. Working in Europe, Jansen and Robert[26] published their findings in this field in 1927. A number of their cases had been treated with iodine, while a number of their cases had not received iodine. A comparative study was made. Table VI is taken from their paper and gives the summary of their results.

Lunde, Closs, and Wülfert,[10] working in Oslo, published in 1929 a paper showing that they obtained the following results:

> Normal human thyroids have an average weight of 20.66 grm. and a total iodine content of 9.86 mg. The relative iodine content is 0.043 for fresh gland and 0.1553 for dried gland. The iodine content of non-toxic adenoma is very variable, yet, in general, greater than the figures already given in the literature. In the secondary hyperthyroid conditions very high iodine values were found for the colloid. In untreated primary hyperthyroid conditions (primary Basedow) the goitre is colloid-poor and iodine-poor. By pre-operative iodine treatment it is changed into a colloid-rich and an iodine-rich gland.

TABLE V.

Relation of Iodine Content of Gland to Minims of Lugol's Solution Administrated

| Group II. | | Group III. | | Group IV. | | Group V. | |
|---|---|---|---|---|---|---|---|
| Minims of Lugol's solution given | Iodine per cent of dried gland | Minims of Lugol's solution given | Iodine per cent of dried gland | Minims of Lugol's solution given | Iodine per cent of dried gland | Minims of Lugol's solution given | Iodine per cent of dried gland |
| 140 | 0.463 | 630 | 0.517 | 140 | 0.429 | 140 | 0.549 |
| 120 | 0.428 | large | 0.496 | 80 | 0.354 | 220 | 0.363 |
| | | 80 | 0.386 | large | 0.309 | large | 0.338 |
| | | 140 | 0.354 | 60 | 0.144 | 120 | 0.273 |
| | | 168 | 0.337 | | | 180 | 0.261 |
| | | 160 | 0.262 | | | 140 | 0.249 |
| | | 40 | 0.251 | | | 72 | 0.140 |
| | | 70 | 0.100 | | | 60 | 0.086 |

TABLE VI.

Verleich zwischen klinischer Diagnose und Jodgehalt

| | | Ohne vorherigen Jodgebrauch | | | | Nach vorherigen Jodgebrauch | | | |
|---|---|---|---|---|---|---|---|---|---|
| Klinische Diagnose | Blut Jodgehalt in γ % Mittelwert | Relativer Jodgehalt der frischen Druse in mg. % | | | Absoluter Jodgehalt in mg. Mittelwert | Relativer Jodgehalt der frischen Druse in mg. % | | | Absoluter Jodgehalt in mg. Mittelwert |
| | | Minimum wert | Maximum wert | Mittelwert | | Minimum wert | Maximum wert | Mittelwert | |
| Normal Schilddrüse | 12–14 | 5.32 | 12.50 | 9.39 | 3.34 | 19.07 | 37.81 | 29.65 | 8.90 |
| Euthyr. Kröpfe. | 4–5 | 0.45 | 9.16 | 4.87 | 6.75 | ..... | ..... | Ca 10.8 | 10.62 |
| Leichte Hyperthyreosea | 18–30 | 4.44 | 5.64 | 5.04 | Ca 7.02 | 2.90 | 6.70 | Ca 4.20 | Ca 8.40 |
| Basedow | 12–40 | 5.37 | 6.81 | 6.09 | 3.41 | 6.37 | 23.91 | Ca 12.00 | 13.11 |

It will be seen that the writer's results confirm these findings. Their series of cases in which the diagnosis of Graves' disease was made was limited to three, and there were only four other cases with toxic symptoms. Their total study was limited to less than 50 cases. and these were mostly colloid and simple goitre.

The present study I believe to be of value because of the wide variation in the cases studied. A large group of patients presenting toxic symptoms has been examined. These patients were available because hyperthyroidism is a relatively common condition in the Manitoba region.

I am greatly indebted to Prof. J. C. B. Grant for facilities for histological study, and to Prof. William Boyd. I am especially indebted to Prof. A. T. Cameron, of the Department of Biochemistry, University of Manitoba, for instruction, co-operation and encouragement.

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# A NEW WHOLE WHEAT IRRADIATED BISCUIT, CONTAINING VITAMINS AND MINERAL ELEMENTS*

BY FREDERICK F. TISDALL, M.D., T. G. H. DRAKE, M.B.,
PEARL SUMMERFELDT, M.B., AND ALAN BROWN, M.B.,

*Toronto*

IN planning a diet it is necessary to have a knowledge not only of caloric requirements and the relative amounts of fats, carbohydrates, and proteins needed but it is also necessary to have a knowledge of the importance of vitamins and mineral elements in metabolism. Before discussing a food product in biscuit form which we have devised we will briefly consider the importance of the vitamins and mineral elements. Deficiencies in these substances are the faults most frequently encountered in our modern diets.

At the present time six separate and distinct vitamins are recognized, and without doubt more will be discovered in the future. The chemical composition of all is as yet unknown. A lack of vitamin A results in deficient growth and the development of xerophthalmia. In addition, this particular deficiency produces a definite alteration in the morphology and function of many of the mucous membranes. Vitamin B has been recently divided into two separate and distinct vitamins; $B_1$, a lack of which causes peripheral neuritis and poor growth; and $B_2$ which is necessary for the prevention of pellagra and certain skin conditions. Vitamin $B_2$ is also necessary for normal growth. Vitamin C prevents scurvy. The antirachitic, or sunshine, vitamin D is necessary for the growth and repair of bone and other tissues. Vitamin E is essential for reproduction, and possibly certain other body changes at the age of puberty.

In addition to producing such definite clinical entities as rickets, tetany, scurvy, and the before mentioned conditions, an inadequate supply of vitamins results in a lowered resistance to infection.[1, 2, 3, 4] We realize that there are many other food factors which influence the resistance of the body cells against disease, such as proteins and mineral elements, but it is evident that a lack of vitamins over a long period may play an important rôle in the development of many of the chronic infective conditions encountered in children and adults.

In regard to degenerative changes it had long been thought that an excess of proteins tends to produce degeneration of the heart, kidneys, and other organs. This idea is now gradually being abandoned, as carefully controlled observations have furnished no evidence in its favour. However degenerative changes do occur in animals fed diets deficient in vitamins, and these changes are sufficient to warrant the belief that an adequate supply of vitamins may be an important factor in the prevention of degenerative changes in human beings. Recent clinical observations lend weight to this belief. Fletcher and Graham[5] have demonstrated the remarkable effect of wheat germ with its high vitamin content in the treatment of chronic arthritis. Boyd, Drain and Nelson[6] have shown the striking results of the administration of a combination of vitamins in the prevention of dental caries and other mouth conditions. Langstroth[7] in a very general paper has advanced some evidence that a lack of vitamins may be associated with arthritis, hypertension, and other degenerative diseases. The importance of focal

* From the Research Laboratories of the Hospital for Sick Children and the Sub-Department of Pædiatrics, University of Toronto, under the direction of Alan Brown, M.B. Presented at the Academy of Medicine, Toronto, January 14, 1930.

infections, however, in the production of degenerative diseases is well known, but, as animal experiments indicate that an inadequate supply of vitamins may be an important factor in the development of these foci of infection, we may conclude that many degenerative diseases may have their origin, either directly or indirectly, in an inadequate supply of vitamins.

It should be remembered that the requirements for vitamins and mineral elements vary greatly, larger amounts being necessary during childhood, and during pregnancy and lactation.

The importance of an adequate supply of the mineral elements, calcium and phosphorus, is universally recognized, particularly for the growth and repair of bone and teeth. Phosphorus is fairly widely distributed, being present in large quantities in meat, eggs, whole grains, milk, and some vegetables. The supply of calcium, however, is more limited, our chief sources being milk and leafy vegetables. McCollum and Simmonds,[8] Sherman and Hawley,[9] and others have shown that the average diet tends to be poor in calcium unless one to two pints of milk are included daily. Although it is obvious that growing children and pregnant or lactating women require large amounts of calcium, it is not so widely recognized that the average adult diet is low in this element unless care is taken to supply it.

Iron is an essential element of the hæmoglobin of the blood and of the chromatin substances within the body cells. Egg yolk has the highest iron content of any food. It is also present in appreciable amounts in liver, lean beef, many fruits and vegetables, and whole grain products. Unfortunately, white flour and finely milled cereals contain very little of this element, as the greater part of the iron is in the discarded germ and bran. Milk contains very little iron. Sherman[10] found that "the typical American dietary does not contain any such surplus of iron as would justify the practice of leaving the supply of this element to chance." It is therefore essential in planning a diet, particularly during infancy and pregnancy, to see that an adequate supply of iron is included.

As recently as one or two years ago it was thought that nine inorganic elements were all that were necessary for life. It can now be said that many others are required. One of the most important of these is copper, minute amounts of which are necessary for the formation of hæmoglobin.

It is obvious that the correct method of planning a diet is first to incorporate in it the essential articles of food, and then to add the non-essential foods in order to cover the remaining caloric requirements. The chief essential foods are milk, meat, eggs, vegetables and fruit. In addition to fats and carbohydrates, these foods supply proteins, vitamins, mineral elements, and roughage. With the knowledge that the average diet, such as white flour, finely milled cereals, sugars, etc., contains an excess of the non-protective or vitamin- and mineral-lacking foods, and realizing the necessity of an adequate supply of these elements we have devised a food product in biscuit form which contains these necessary substances in appreciable quantities. Where the ordinary biscuit, zwiebach, rusk, toast or bread are all low in proteins, lacking in vitamins, and deficient in calcium, iron, and other salts, this biscuit contains in appreciable quantities most of the food elements necessary for the growth and repair of body cells and the maintenance of resistance against disease. The biscuit has as its basis whole wheat flour, irradiated wheat germ, milk, bone meal and iron. The whole wheat is in the form of a finely ground flour. The milk is added as a milk powder.

In regard to wheat germ, which constitutes 15 per cent of the biscuit, it is well to mention here the place it occupies in the structure of a grain of wheat. Due to the present day desire for only finely milled products the germ is ordinarily discarded and not used for human consumption. The whole grain consists of three well defined structures, the bran, the endosperm, and the germ. The bran which constitutes about 13.5 per cent of the wheat acts as a protective layer for the rest of the grain. It is comparatively rich in proteins, phosphates and vitamins. The endosperm which furnishes food for the germ during growth and makes up about 85 per cent of the grain is the portion which is utilized in the manufacture of white flour and finely milled cereals. It is very poor in mineral elements and is devoid of vitamins. The germ constitutes only about 1.5 per cent of the grain and is the living part of the seed which grows and develops into the new plant. The germ contains about 8 per cent fat and 30

per cent protein. Its mineral content is about double that of the whole wheat flour and ten times that of white flour. It contains in appreciable quantities vitamins A, $B_1$, and $B_2$, and is the most concentrated source known of the reproductive vitamin E.

Before the wheat germ is used in the biscuit it is exposed to the rays from a mercury quartz lamp. As discovered by Steenbock,[11] these rays activate the ergosterol normally present in the germ and thus produce the antirachitic, or sunshine, vitamin D. The whole wheat flour and germ used in our product thus contains all the known vitamins with the exception of the antiscorbutic vitamin C found in fresh orange juice. The vitamin content is further increased by the use of some butter and yeast. Butter supplies vitamin A in large quantities and yeast is a highly concentrated source of both vitamin $B_1$ and $B_2$. The yeast is not used as a leavening reagent but as a source of vitamins.

The bone meal is obtained by cooking bones in an autoclave at 267° F. for five hours. This removes all the fat. The bones are then ground and dried in an oven at 220° F. for twelve hours. The final product is an odourless and tasteless white powder. We are using this product in preference to the chemical substance calcium phosphate as there are traces of other mineral elements in the bone meal which may be of importance in the mineral metabolism of the body. The bone meal constitutes about 3 per cent of the biscuit. This means that five to six biscuits have the calcium content of one pint of milk. The iron content is about 5 mgs. iron per 100 grams of biscuit as compared to about double this amount in egg yolk, our most concentrated source of iron in food. The iron is largely obtained from the wheat germ and whole wheat. Examination of the biscuit shows the presence of copper in the concentration of about 1 mg. per 100 grams of biscuit.

In studying the vitamin D content of the biscuit it was found that a considerable amount of the vitamin D present in the irradiated germ before cooking was destroyed when the biscuit

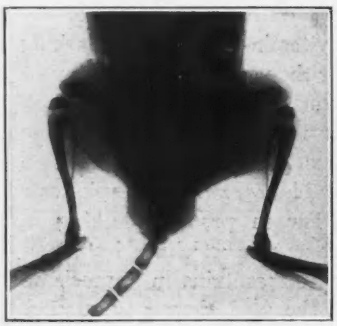

FIG. 1. — Roentgenogram of rat fed on a rachitogenic diet +25 per cent non-irradiated biscuit. Blood phosphorus 1.1 mgm. per 100 c.c., and bone ash 37.2 per cent.

FIG. 2.—Roentgenogram of rat fed on a rachitogenic diet +25 per cent irradiated biscuit cooked at 425° F. Blood phosphorus 2.4 mgm. per 100 c.c. and bone ash 37.8 per cent.

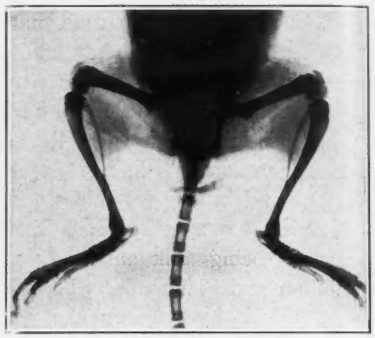

FIG. 3.—Roentgenogram of rat fed on a rachitogenic diet +25 per cent irradiated biscuit cooked at 300° F. Blood phosphorus 3.0 mgm. per 100 c.c. and bone ash 48.7 per cent.

TABLE I

THE ANTIRACHITIC EFFECT OF IRRADIATION OF FOOD AND SUBSEQUENT COOKING AT DIFFERENT TEMPERATURES

| | *Mgm. P. per 100 c.c. of blood* | *Percentage of ash in bones* |
|---|---|---|
| Rat on normal diet; age 8 weeks.. | 6.3 | 57.0 |
| Rat on Steenbock's rachitogenic diet ..... | 1.0 | 32.5 |
| Rat on rachitogenic diet + 25 per cent of non-irradiated biscuit* | 1.1 | 39.0 |
| Rat on rachitogenic diet + 25 per cent of irradiated biscuit cooked at 425° F.* ..... | 2.4 | 37.8 |
| Rat on rachitogenic diet + 25 per cent of irradiated biscuit cooked at 300° F.* ..... | 3.0 | 48.7 |
| Rat on rachitogenic diet + 25 per cent of irradiated whole wheat and germ in proportions used in the biscuit, uncooked* .. | 3.0 | 46.5 |
| Maximum antirachitic effect possible with rats on rachitogenic diet with the use of ordinary therapeutic measures ..... | 4.5 (about) | 54.0 (about) |

* 76 per cent of the rachitogenic diet consists of yellow corn. The material to be tested was substituted for an equivalent amount of corn.

was baked at 425° F. the temperature ordinarily used in baking biscuits. It is quite possible that if the amount of vitamin D produced by irradiation is markedly increased sufficient amounts for practical purposes may escape destruction at this temperature. After experimenting with different temperatures it was found that very little of the vitamin D was destroyed when the temperature of baking did not exceed 300° F. This is shown by the results in Table I and Figs. 1, 2 and 3. We estimate that the vitamin D content of ten to twelve biscuits is equal to that of one teaspoonful of standard cod liver oil.

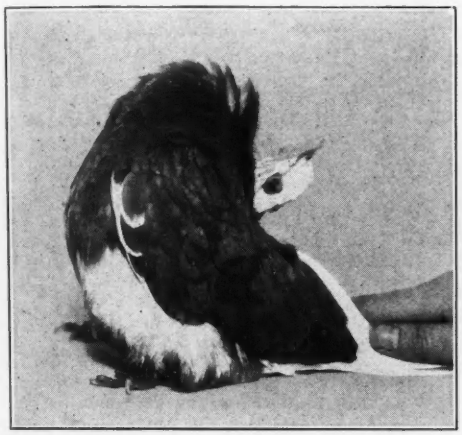

FIG. 4.—Pigeon fed on a diet deficient in vitamins $B_1$ and $B_2$. After 4 weeks it developed polyneuritis, or beriberi, and died.

Fig. 4 is that of a pigeon fed on a diet deficient in vitamin $B_1$ and $B_2$. After 4 weeks it developed polyneuritis, or beriberi, and died. Fig. 5 is that of another pigeon fed on the same diet, but in addition it received 15 per cent of wheat germ cooked at 300° F. for 20 minutes. After eight weeks on this diet it was apparently normal. Fig. 6 is that of two rats, the smaller one being fed for 4 weeks on a diet deficient in vitamin $B_1$ and $B_2$, and the larger rat was fed on the same diet, but in addition received 15 per cent of the cooked wheat germ. This demonstrates that the heat condition under which the biscuits are cooked does not entirely destroy vitamin $B_1$ and $B_2$.

It is the custom in the manufacture of biscuits to add certain alkaline salts as leavening agents. This produces an alkaline reaction which readily destroys vitamin $B_1$ and $B_2$ during cooking. To overcome this we have produced a biscuit with a reaction just on the acid side of neutrality through the addition of a small amount of cream of tartar. Further observations are underway to determine the exact concentration of each vitamin in the biscuit.

We would like to emphasize that no attempt should be made to supply all the vitamin requirements with this biscuit. Cod liver oil should still be administered to infants and children, to supply vitamins A and D. The diet should still be constructed around the essential articles of food, namely, milk, eggs, meat,

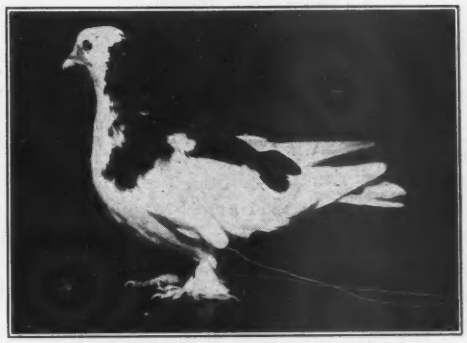

FIG. 5—Pigeon fed on a diet deficient in vitamins $B_1$ and $B_2$ with 15 per cent of wheat germ added. The wheat germ was cooked at 300° F. for 20 minutes. After eight weeks on this diet the bird was apparently normal.

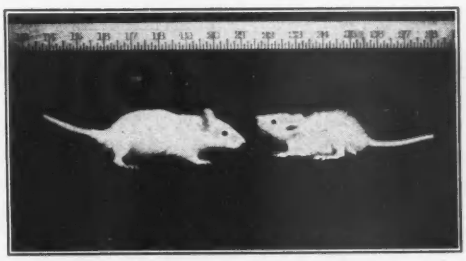

FIG. 6.—Two rats fed on a diet deficient in vitamins $B_1$ and $B_2$. The larger rat received in addition 15 per cent wheat germ cooked at 300° F. for 20 minutes.

vegetables and fruit. But when the biscuit is used in place of the ordinary biscuit, rusk, zwieback, toast or bread, in addition to simply supplying calories, a food will be given which will assist in the repair and growth of body cells and the maintenance of resistance against disease.

With the realization that our work is only partly completed unless this biscuit is manufactured under the conditions outlined and made available to the public, we have arranged with the McCormick Manufacturing Company to produce this biscuit under our supervision.

XUM

It will shortly be available under the trade name of McCormick's Sun Wheat Biscuit.*


### SUMMARY

A biscuit has been devised containing whole wheat, wheat germ, milk, butter, yeast, bone meal, iron and copper.

The wheat germ contains a large amount of vitamin E and appreciable amounts of vitamin A, $B_1$ and $B_2$. In addition it has been exposed to the rays of a mercury quartz lamp which activates the ergosterol present and thus produces the antirachitic vitamin D. Vitamin A is present in large amounts in the butter, and yeast is a concentrated source of vitamins $B_1$ and $B_2$.

The biscuit is baked under conditions which conserve the vitamin content.

Bone meal is added to supply calcium and phosphorus. Five to six biscuits contain the same amount of calcium as one pint of milk, the most important food source of this element.

The iron content is approximately one-half the concentration found in egg yolk, our highest source of iron in food. A trace of copper is also present.

The biscuit should be regarded as belonging to the essential or protective class of foods, and may be used to replace the ordinary biscuit, rusk, zwiebach, toast, or bread which are non-protective foods.


* The patents for the manufacture of this biscuit are held by the Research Laboratories, and all royalties accruing will be devoted to medical research.

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## SURGICAL MEASURES IN THE TREATMENT OF PULMONARY TUBERCULOSIS*


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THE treatment of pulmonary tuberculosis by artificial pneumothorax was barely established on this continent when the surgeon entered the field to help make good its failures. To Dr. E. W. Archibald, as a pioneer in introducing thoracoplastic methods to America, and to Dr. John Alexander, for his illuminating survey of a vast literature, thereby hastening their adoption, a great debt of gratitude is owing from both physicians and patients. I had the good fortune to have Dr. Archibald accessible, although at long range, and I am grateful to him for the successful results obtained in the earlier days when patients were persuaded with some difficulty to undergo what seemed an appalling operation, uncertain in outcome. I am also indebted to Dr. N. S. Shenstone for undertaking more recently some very unpromising material with the hope of palliation, and for doing the series of phrenicotomies.

Something may be gained by the analysis of this small amount of material in regard to the indications for the operations and to the factors of resistance, and by a re-appraisal of the points upon which selection was based.

During the twelve years since 1916, compression of the lung by artificial pneumothorax has been attempted in 141 patients, that is in 22 per cent of all tuberculous patients under treatment, or in 28 per cent of the moderately- and far-advanced cases.

Satisfactory compression was impossible in 63 patients (45 per cent of the cases attempted),

* Read at the forty-fourth annual meeting of the Association of American Physicians, at Atlantic City, May 7, 1929.

and 27 of these (43 per cent) underwent further operations (thoracotomy in 5 and thoracoplasty in 23). Thirty-four patients also had phrenicotomies (9 per cent of all patients during five years since 1923).

A thoracotomy for the division of adhesions, to improve an incomplete artificial pneumothorax, was done in 5 cases. Although successful in improving the pneumothorax, all developed pleural effusions; 3 of these were transitory, but 2 became tuberculous empyemata; and in 1 a streptococcal infection developed, probably from the cut adhesion, and only strenuous treatment brought about an ultimately good result. This method is fraught with danger. When facilities for the cauterization of adhesions by the method of Jacobæus, ardently advocated and effectively used by Matson, are not available, the substitution of thoracoplasty would in many cases be preferable.

Thoracoplasty has been undertaken in 23 cases, or in 3.5 per cent of all tuberculous patients (in 6.5 per cent of the far-advanced cases, and in 16.3 per cent of all attempted artificial pneumothorax cases). Four of the operations were for tuberculous empyema. In the majority the complete two-stage operation of Sauerbruch was done. A supplementary apicolysis, for compression of a cavity, was done in 2 cases, and further rib resections for empyema in 2 cases. In only 2 of the 45 operations were local anæsthetics used alone without gas and oxygen. Accessory radical phrenicotomies were done in 7 of these patients.

Of the 23 thoracoplasties, fair compression only was obtained in 6, good in 10, and excellent in 7. The good results obtained in some of the earlier, less effective, compressions were remarkable, but when there are large cavities the result has usually been proportionate to the reduction in volume of the lung.

The early results obtained from the operation (see table) were: 1 dead, directly due to operation; 1 worse, due to secondary infection of a tuberculous empyema; 5 little changed, owing to short time since operation; 6 improved; and 10 arrested. The term "arrested" implies absence of bacilli, absence of constitutional symptoms, and fair working capacity.

Changes in condition have inevitably occurred

TABLE

RESULTS OF THORACOPLASTY IN TWENTY-THREE PATIENTS, FROM 1917 TO 1928.

| | *Early results* | *Length of life since operation* | *Present results* |
|---|---|---|---|
| DEAD: | 1=4.3% | .... | 6=26% |
| Directly due to operation: | | | |
| 1 cardiorespiratory failure | .... | 6 days | .... |
| From causes not due to operation: | | | |
| Nontuberculous: | | | |
| 1 typhoid fever (tentative status, unchanged) | .... | 7 weeks | .... |
| 1 pneumonia (tentative status, arrested) | .... | 6⅓ years | .... |
| Tuberculosis: | .... | Aver. 4⅓ years | .... |
| 1 intestinal (tentative status, some improvement) | .... | 1½ years | .... |
| 1 progressive pulmonary (tentative status, much improved) | .... | 6½ years | .... |
| 1 progressive pulmonary, hæmoptysis and pneumonia (tentative status, much improved) | .... | 5 years | .... |
| FAILED: | .... | .... | 1= 4.3% |
| 1 after 3 years (tentative status, much improved) | .... | 3¼ years | .... |
| WORSE: Immediate result of operation: | 1= 4.3% | .... | 1= 4.3% |
| 1 tuberculous empyema, strepto. infection | .... | 1½ years | .... |
| UNCHANGED: | 2= 8.7% | .... | 1= 4.3% |
| 1 (transferred to "dead" group) | .... | .... | .... |
| 1 | .... | 6 months | .... |
| SOME IMPROVEMENT: | 3=13.0% | .... | 2= 8.7% |
| 1 (transferred to "dead" group) | .... | .... | .... |
| 1 (1½ years, ½ year) | .... | Aver. 1 year | .... |
| MUCH IMPROVED (3 lost B. tuberculosis and 4 have considerable liberty): | 6=26.0% | .... | 3=13.0% |
| 2 (transferred to "dead" group) | .... | .... | .... |
| 1 (transferred to "failed" group) | .... | .... | .... |
| 3 (5⅔, 5½, 5/6 year) | .... | Aver. 4 years | .... |
| ARRESTED: Successful (without B. tuberculosis, and at work): | 10=43% | .... | 9=39.0% |
| 1 (transferred to "dead" group) | .... | .... | .... |
| 9 (12⅓, 6, 6, 6, 5, 4½, 4½, 3¾, 3½ years) | .... | Aver. 5¾ years | .... |

Average length of life since operation: of all cases, 3.9 years; of 17 living, 4.2 years; of 6 dead, 3.25 years.

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during the twelve years, and present results show 6 dead; 2 from non-tuberculous disease, 3 from progressive tuberculosis; 1 relapsing; 1 worse; 1 unchanged; 2 somewhat improved; 3 much improved; and 9 arrested.

In the early group, 69 per cent obtained good results (26 per cent being improved and 43 per cent arrested), and up to the present 52 per cent have maintained their position (13 per cent much improved and 39 per cent arrested).

The average life of all cases since operation has been 3.9 years; of the 17 living, 4.2 years; of the 6 dead, 3.25 years. The longest life has been 12.5 years. The sputum became negative in 12 of 21 patients (57 per cent) who had positive sputum immediately before operation.

Temporary activity in the better lung shortly after operation occurred in 1 case, after 1 year in a second, and after 5 years in a third. Progressive disease has occurred in 4, and 3 of these have died. Complications, either tuberculous or nontuberculous, have not appreciably influenced the results.

Twenty of the 23 patients have been satisfied with the result of the operation, and the majority delighted; 1, much disappointed that she was not entirely free of sputum, lost the opportunity given by the operation through indiscretions; and 1 is naturally dissatisfied because of chronic infection of a tuberculous empyema. These 2 patients were relatively young and their resistance poor, compared with their apparent vitality.

The grouping of patients, according to the indications for operation, shows in the results, the possibilities and limitations of thoracoplasty. The special indication, *i.e.*, the character and extent of the disease, suitable, with no contra-indications, gave in the early results 80 per cent of arrested successful cases, and 10 per cent much improved, partially successful. The relative indication, *i.e.*, the disease suitable, with doubt regarding contraindications, or less suitable with no definite contraindications, gave 25 per cent successful and 25 per cent partially successful results. The symptomatic indication gave only 60 per cent partially successful results.

A preliminary pneumothorax should always be attempted. If successful, the thoracoplasty is avoided; if partially successful, certain very distinct advantages are gained for the ultimate thoracoplasty, and the surgeon is warned as to the condition of the pleura. The one fatality due to operation probably resulted from my failure to observe this rule—the only case in which pneumothorax had not been attempted. A partial pneumothorax has been of great value to the majority of patients in this series because it furthers fibrotic changes and contraction. Caseating lesions have thus been put on more even terms with the more suitable fibrous forms, and the results obtained in the two groups have been identical. The mediastinum, also, usually becomes less flexible, and, if still flexible, the heart has at least become accustomed to displacement. The pleura has become thickened, and the chance of injuring it at operation is less. The opposite lung has been on trial, and if any lesion exists therein this has improved because of the resulting constitutional improvement. When pneumothorax exists at the time of the operation, the cut ribs fall in more easily, a good collapse is readily obtained and post-operative symptoms are usually less marked.

Success depends upon the selection of the case, the judgment and skill of the surgeon, the management of the patient before and after operation, a reasonable period of protecting after-care, and the subsequent morale of and the restraint exercised by the patient.

Thoracoplasty is indicated in several kinds of lesions when the opposite lung shows but little evidence of disease, and that presumably inactive or but very indolently active, if there are no serious contra-indications, especially in heart or kidneys, and if vitality is not too greatly impaired. It should replace pneumothorax if, for any reason, the compression of a severely diseased lung cannot be continued, provided the opposite lung has proved its ability to endure. It is in most cases the logical treatment of the tuberculous empyema following artificial and spontaneous pneumothorax, because repeated aspirations lead to abscess formation along the needle-track and to secondary infection.

The resistance of the patient is of supreme importance in the matter of selection, and the several factors which make him suitable for operation point to a relatively high degree of resistance. One index of this resistance is the character of the disease in the bad lung. Fibrotic changes, with evidences of contraction, as shown by altered contours, the displacement

of the heart, mediastinum and trachea, and compensating emphysema, are essential indications. The ability to repair and to endure are thereby shown. These cases will usually have some degree of cavity formation. With such signs of long resistance, even relaped cases with recent massive infiltration have improved extraordinarily after a thoracoplasty and may be considered possibilities. Fibrocaseous disease, with little evidence of fibrosis and contraction, is a more doubtful risk, and acute exudative lesions without marked past evidence of fibrosis have not been considered.

A second index of resistance is limited disease in the better lung. If not strictly limited, the failure of resistance is self-evident. Partly by good fortune, to some extent by care (rest or artificial pneumothorax), but most probably by acquired resistance, the opposite lung has been protected, although there has been long and great opportunity for its involvement. Healed processes in the better lung point strongly to a relatively high local resistance. In exceptional cases, even when the healed areas in the better lung show more than minimal involvement, operation on a worthless lung may be justified, since the better lung has proved its ability to endure. Extraordinary local relative immunity has been developed; indeed, the original pulmonary lesion may have been in the better lung and relapses have occurred in the now worse lung, which is usually the left. In the cases selected lesions in the better lung have been, with one exception, considered minimal in extent and character in x-ray films (Trudeau Sanatorium standards), and physical signs have been absent or slight. One-half of the lesions were above the second rib and one-half beyond this limit.

Time is required to make the "good chronic" (Archibald) desired by the surgeon, and becomes a factor in resistance. The least favourable results in this series have been found in the group of patients between 20 and 29 years of age, and in the group of patients in whom the duration of disease was less than 5 years, most of whom fell in this decade. Results improved proportionately in each 5-year period of duration up to 20 years since onset. (It is recognized that the numbers are too small to be other than suggestive). The interval between the onset of disease and the last disabling breakdown seems also of moment. The longer the interval the better the resistance, and the more warranted operative interference in case of further invasion of the bad lung. Acquired resistance, with the demonstrated ability to endure, scores over the vitality of youth with insufficiently developed acquired resistance. Shortness of duration can be offset to some extent, and the changes of chronicity furthered, when artificial pneumothorax of moderate extent can be induced.

A number of individual characteristics are factors in resistance, such as race, sex, complexion, family physique and longevity, and family tuberculosis. Conditions of impaired vitality and function demand cautious analysis as to cause, and an estimate of the probable effects of operation upon them, for they may have an important bearing upon the selection of the patient for operation. Possibly there has been too great local or constitutional damage for the operation to be worth while. Such conditions are dyspnœa, cyanosis, tachycardia, malnutrition, dyspepsia, anæmia and cachexia. Although tuberculous laryngitis and colitis are further evidences of impaired resistance, if only slight they need not be considered contra-indications. They will probably benefit from the constitutional improvement resulting from the thoracoplasty. Disease of the heart or kidneys, as previously mentioned, requires careful consideration as to the possible effect of operation upon them.

The majority of patients for whom there is a special indication for thoracoplasty are fairly obvious cases, and have qualified for the finals, so to speak, justifying the opportunity by the character of the disease in the bad lung and the slight evidence of disease in the opposite lung, both the result of resistance. Their competitors for the privilege have been eliminated through failure to protect the better lung.

Restraint in the selection of questionable risks is desirable, and exceptional conditions only may justify great risk. Restraint is urged not only in the interest of the patient under consideration but for the benefit of the many suitable patients who will ultimately be considered for thoracoplasty. Good results from operation should not be burdened by many failures. The statistics relating to the operation should become an encouragement for likely candidates. Moreover, with steadily increasing numbers of pa-

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tients referred for thoracoplasty, surgeons should be relieved of taxing operations that will not bring about results worth while. The surgeon's demand is for an earlier lesion and a better type of patient. He would have the patient, if suitable, submitted at once for thoracoplasty when artificial pneumothorax cannot be induced. Such a rule would, however, have many exceptions, especially in the case of women.

The possibility of evading thoracoplasty, at least temporarily, by phrenic evulsion is to be considered. This procedure is worth trying, and if thoracoplasty must follow, the trial of the better lung will have been reassuring and a useful accessory to the thoracoplasty accomplished. Since early in 1924 phrenicotomies have been done on 34 patients for various conditions, as a curative, palliative, or precautionary measure, and as a supplement to artificial pneumothorax or thoracoplasty. The objective attempted was reached in 41 per cent; improvement resulted in 35 per cent; and failure in 24 per cent.

The phrenic evulsion of Felix was the method used with all but 2 patients. Gas with oxygen was given for one-half of the operations, as there is often considerable pain on withdrawal of the nerve after the lung has been long compressed. No material complications arose from the operation. In one case there was slight impairment of sympathetic fibres, as shown by irregular lacrimation, vascular engorgement of the left cheek, and slight contraction of the pupil. These symptoms have persisted for a year. Respiratory embarrassment has been extremely slight, and serves as a warning in regard to exertion. Early slight difficulties of defæcation have been complained of. Slight nausea and loss of appetite have been persistent in one right-sided case. The most frequent complaint has been some discomfort from the collection of gas under the left dome of the diaphragm. Elevation of the diaphragm (measured by projection on the x-ray film) was high in 3 cases (7 to 10.5 cm.); moderate in 22 (3.5 to 7cm.); and slight in 9 (1 to 3.5 cm.).

In a group of 13 cases, undertaken with the hope of arresting or controlling the disease, the results achieved were: success in 6; much improvement in 4; and failure in 3. Six patients lost bacilli. Nine apical lesions showed contraction, a large cavity disappearing entirely in 1; and further operation (artificial pneumothorax or thoracoplasty) was avoided in 7 cases. For the relief of symptoms in hopeless cases, it was very helpful in relieving cough in 4 out of 6 cases, but failed to prevent recurrent hæmorrhage in one case with a large cavity.

As an accessory to artificial pneumothorax, to lessen cough due to adhesions and to lessen the frequency of refills, it gave marked relief in 2, and some improvement also in 2 out of 6 cases. It has helped at the same time to make an incomplete pneumothorax more effective. Upon discontinuing the pneumothorax, in 3 cases it has been used to prevent undue re-expansion of the compressed lung, and to aid intrathoracic adjustments.

As an accessory to thoracoplasty, one operation immediately preceding showed no result. Marked relief to tachycardia followed in 1 case in which, after an upper thoracoplasty, an existing partial pneumothorax was continued. In 5 cases having only an incomplete compression of the lower lobe, with cough or blood-spitting persisting, it was effective in 3 in relieving symptoms, and caused marked improvement in 2. As a precautionary measure against relapse after long sanatorium treatment it has been done once, with apparently successful result.

The crushing or evulsion of the phrenic nerve is a valuable accessory in treatment and has wide application. The compromise in result obtained by its use alone may be sufficient to enable some patients to attain and maintain a satisfactory state of health, but, if after a reasonble trial the result is disappointing, in those patients for whom either artificial pneumothorax or thoracoplasty is indicated, these operations should not be long delayed.

## COMMENTS

An experience of more than twelve years with these surgical procedures has established my faith in their value to the tuberculous, if a careful selection of patients is made. Surgical aid, furthering rest to a severely diseased lung, thereby favouring curative processes, has given a high proportion of success in obtaining the result desired.

The durability of the results from extrapleural thoracoplasty has been surprising, none of the arrested cases (43 per cent of the series) having relapsed. One patient, operated on

twelve and a half years ago, is still well and working, and was probably the first successful case of extrapleural thoracoplasty on this continent. The results obtained by phenicotomy have been gratifying. For various conditions the objective attempted was reached in 41 per cent.

The physician must have sufficient opportunity for the thorough study of the candidate for one of these operations. He must have opportunity to study the course of the disease, the physical reactions of the patient during illness, the evidences that the physical signs give of the underlying pathological condition, and thus be able to make a fair estimate of the result of the operative procedure for the welfare of the patient.

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## THE TREATMENT OF IDIOPATHIC (HYPOCHROMIC) ANÆMIA WITH IRON AND COPPER*

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THE following communication is a preliminary report of the beneficial effect of combining small quantities of a copper salt with iron for the treatment of idiopathic anæmia of the hypochromic type. So far as it can be ascertained from the literature, copper and iron mixtures have never been prescribed for the treatment of this disease though their effect on experimental anæmia in animals has been demonstrated recently by two independent research groups.[1, 2, 3] The effect of other inorganic substances than copper added to iron for treating experimental anæmia has been found to be slight or nil.[4]

*1. The type of anæmia.*—About the time that Hart and his co-workers[1] reported the results of their investigations on the treatment of nutritional anæmia in white rats, the author was engaged in searching for an effective method of treating a group of cases of secondary anæmia of undetermined etiology which had proved resistant to liver feeding and to ordinary iron therapy. Such cases have been referred to recently in the literature under the rather paradoxical title of idiopathic secondary anæmia. In view of their unknown etiology and because the colour-index is low, hypochromic would seem to be a better term than secondary. In our experience, this disease invariably begins in women between the ages of 20 and 40. The symptoms complained of are usually weakness, lassitude, pains in the back, and numbness or tingling in the extremities, a common story in any type of anæmia. There is sometimes a history of anæmia in other members of the family, as in two of the cases reported. Examination reveals a waxy or subicteroid pallor with some atrophy of the tongue, but rarely enlargement of the spleen, and never definite subacute combined sclerosis of the cord. There is usually, though not invariably, achlorhydria. The blood shows little or no reduction in the number of erythrocytes, but they are smaller than normal and reticulocytes are scanty. The striking feature of the red cells is their pallor, hence the extremely low colour-index. The leucocytes are normal or slightly reduced in number at the expense of the polynuclears. The plasma is pale and does not give the van den Bergh reaction. Exhaustive clinical and laboratory studies otherwise prove negative.

One of the most striking features of this type of anæmia is its chronicity. The onset may be rapid during pregnancy or in the post-partum state, or so slow as to be observed first by the physician when he is consulted about the resulting weakness. Once established, the anæmia usually persists for years uninfluenced by ordinary treatment. Most of the cases which we have seen gave a history of treatment over periods from five to ten years. Two cases were actually observed in the clinic for four and five years respectively. They are unlike post-partum anæmia, as described by Osler, and chlorosis, chiefly because they resist treatment. They differ

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from Addisonian anæmia in the following respects: (a) they do not show cord changes or the blood picture of this disease; (b) achlorhydria is not a constant feature. Many of the cases have been called aplastic anæmia, incorrectly, because that disease tends to run a progressively downhill course. In these cases, on the contrary, the hæmoglobin undergoes a reduction to a certain level, often in the vicinity of 50 per cent, and persists at that low level for long periods. It would thus seem that the disease is one of the hæmoglobin-producing mechanism, whatever that may be.

*2. The effect of large quantities of iron.*—Early in 1928 the effect of rather large doses (75 grains daily) of iron in the form of Blaud's capsules was tried on a group of these cases with only partial success. Some cases showed decided improvement, especially when it was combined with a diet containing liver. Other cases were tried on liver alone without remarkable results. Many of the patients quickly tired of the liver and whatever improvement they had shown was soon lost. On the whole, the results were far from encouraging, and the few partial successes were explained on the basis of chance.

*3. The effect of an iron-vitamine concentrate derived from liver.*—At the request of a pharmaceutical house these cases were placed upon capsules containing iron and a concentrated form of vitamin E (Ferrum E) but without any appreciable benefit. (cf. Charts I and II).

*4. The effect of capsules of Blaud's with copper.*—After the publication of the effect of copper and iron mixtures in the treatment of experimental anæmias in animals,[1] it occurred to us to try the effect of copper-iron mixtures on these cases of idiopathic hypochromic anæmia. The toxicity of copper for man has been a matter of much controversy,[5] but recent reports indicate that fairly large amounts may be given by mouth without fear of any untoward effects. Any local effects on the mucous membrane of the intestinal tract are so slight as to be disregarded when such small amounts are employed.

With the co-operation of a local drug manufacturer a capsule was made up to contain Blaud's mass grm. 2, copper sulphate mg. 1.5 and phenolphthalein grm. 0.017. Three capsules were prescribed daily. The phenolphthalein was added to prevent the constipating effect of the iron but proved too laxative. The resulting diarrhœa aggravated the anæmia (cf. Charts I and II). In the second lot of capsules the phenolphthalein was replaced by cascara with good results. The clinical course of four of the 10 cases tried on this preparation may be summarized as follows.

### CASE 1

Mrs. C. C., aged 37, first came under observation in May, 1926, complaining of tingling in the extremities, weakness, and anæmia of two years' duration, beginning post-partum. On examination the features were: subicteroid anæmia, slight atrophy of the tongue, and a palpable spleen but no cord changes. Test meal revealed free HCl 14 and total acidity of 33. Barium series and basal rate were normal. The blood Wassermann and the van den Bergh reaction were negative. The blood examination showed red blood cells 3,790,000, white blood cells 4,950, hæmoglobin 47 per cent (Hellige). Shortly after this she was hospitalized and placed on a liver diet with definite improvement. She tired of the liver and refused to take it so was placed on liver extract, following which her hæmoglobin gradually dropped from the maximum of 78 per cent while on whole liver, to 50 per cent at which level it was on February 5, 1929.

CHART I

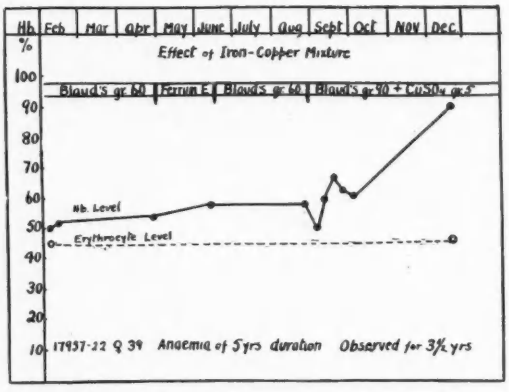



Chart I shows briefly the course during the next year. The initial drop immediately following iron-copper therapy was associated with diarrhœa due to excessive phenolphthalein in the capsules. As regards her present health, she was seen last on December 17, 1929, when she stated that she felt better than for the last five years. She has lost the feeling of weakness and has gained 16 pounds in weight.

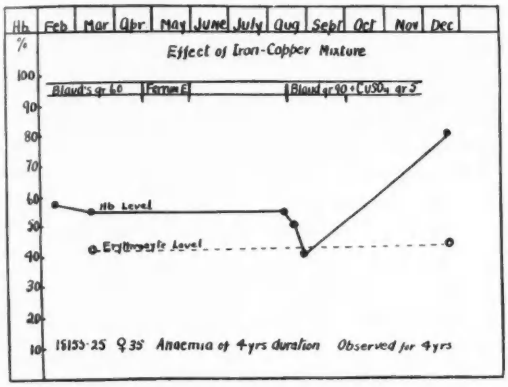
### CASE 2

Mrs. O. J., aged 31, was first seen in November, 1925, because of weakness and tingling in the extremities dating from a pregnancy 6 months before. There had been no undue loss of blood at delivery. Examination on November 10, 1925, revealed a waxy pallor of skin and mucous membranes, an atrophic tongue, but no enlargement of the spleen and no combined sclerosis of the cord. Barium series and basal rate were normal. The van den Bergh and Wassermann reactions were negative. The blood picture was as follows. Red blood cells 3,560,000, white blood cells 7,000, hæmoglobin 50 per cent. In spite of treatment by Blaud's and other iron mixtures she remained at about this level until May 20, 1928, when the blood examination showed red blood

* In all charts read mg. 5 $CuSO_4$ for gr. 5.

cells 4,400,000, white blood cells 8,000, hæmoglobin 45 per cent. During May and June of that year she was placed on calf's liver and Blaud's with striking improvement, the hæmoglobin rising to 88 per cent. She tired of liver, however, and ceased to take it regularly. On February 12, 1929, her hæmoglobin was again down

CHART II



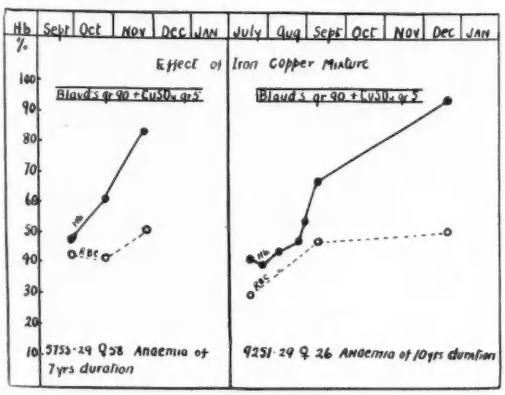

to 58 per cent. The subsequent course is illustrated by Chart II. As in case 1, a drop in the hæmoglobin was noted during a period of diarrhœa. At the present time she is so well that she considers herself cured and is with difficulty persuaded to return to the hospital for observation.

CASE 3

Mrs. C. M., aged 58, was first seen on September 26, 1929, because of weakness and anæmia of seven years' duration. She had been treated by oral and hypodermic administration of iron over a period of three years without improvement. It is of interest that her father died of anæmia. On examination she presented a subicteroid pallor and some atrophy of the tongue but no enlargement of the spleen or cord changes. Barium series and basal rate were normal. Ewald test meal showed achlorhydria. The Wassermann and van den Bergh reactions were negative. The blood count was as follows. Red blood cells 4,330,000, white blood cells 3,700, hæmoglobin 48 per cent. She was placed on the iron-copper capsules, and when she reported after a fortnight she had gained weight and felt decidedly better. Chart III shows the improvement in the blood picture. At the present time, after three months' treatment she is well and her blood picture is practically normal.

CHART III

CHART IV




CASE 4

H. F., aged 26, was referred to the medical clinic on July 15, 1929, because of anæmia and a sudden retinal hæmorrhage. The history was that she was first treated for anæmia ten years ago by means of Blaud's pills with some improvement. However, three years ago the anæmia became more severe, and she had difficulty in doing her duties as a domestic because of weakness and shortness of breath. Examination on July 15, 1929, was negative except for the marked waxy pallor and the retinal hæmorrhage. There were no splenic enlargement or cord changes. The blood Wassermann test, van den Bergh reaction, and barium series were all negative. An Ewald meal on three occasions showed achlorhydria. As shown by Chart IV improvement on the iron-copper capsules was rapid and complete. She has gained 20 pounds in weight and feels well. On December 18, 1929, the red blood cells were 5,050,000, the white blood cells 6,000, and the hæmoglobin 94 per cent.

## DISCUSSION OF RESULTS

The foregoing cases are representative of a series of ten cases of idiopathic hypochromic anæmia treated by means of an iron-copper mixture. They are not "picked" cases. All remaining cases have shown similar results and promise to compare favourably with those reported. One case has been slow in showing improvement due to a recent bleeding uterine polyp.

It is of interest that several of the cases showed distinct though temporary improvement when taking Blaud's capsules along with a diet containing calf's liver. In the light of the results obtained from Blaud's and copper, it would seem that the beneficial effect of the liver-Blaud combination was due to the copper content of the liver which is considerable, according to a recent analysis 145 mgm. per kilo of fresh liver.[6]

Any explanation as to why copper is of such value when combined with iron in the treatment of these cases is largely speculation. It may be a catalyst as Waddell and his coworkers suggest.[1] Certain of its salts are known to be good catalysts *in vitro* and recent observations on the oxygen-combining power of dog's blood after heavy copper feeding suggest that it may have this same catalytic action in the circulating blood. Whether iron-copper feeding will throw any light on the cause of the anæmia under discussion remains to be seen. It would seem that the secret of the success of iron-copper therapy will only be revealed by a better understanding of the chemical nature and method of production of the hæmoglobin molecule.

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SUMMARY AND CONCLUSIONS

Idiopathic anæmia of the hypochromic type tends to persist for years unless treated.

In our experience, treatment by iron alone or combined with vitamine E is not effective in raising the hæmoglobin level appreciably in these cases.

Cases of this disease of long duration were treated with a combination of iron and copper given in capsules by mouth. Prompt improvement followed in all cases with restoration of the blood to about its normal level.

The improvement noted in two of our cases during a period when Blaud's and calf's liver were given simultaneously may be explained on the basis of the high copper content of the liver.

(The author wishes to express his appreciation of the assistance of Dr. Evans of the Montreal General Hospital, and of the Charles E. Frosst Company for preparing and donating the capsules.)

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# THE PATHOLOGY OF CERVICAL ECTROPION (CERVICAL EROSION)

BY J. R. GOODALL, O.B.E., B.A., M.D., C.M., D.SC., F.A.C.S

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THE ectropion visible as a zone of redness and granulation about the cervical canal is variously described in text-books as eversion, erosion, ulceration, and outgrowth of the cervical mucosa. It is associated usually with one symptom, leucorrhœa, due not to the ectropion but to the associated and causative chronic endocervicitis. The work that is now to be described constitutes a new chapter in the pathology of the cervix. The conclusions have been drawn from the study of material removed at operation, and from the study of cases before treatment and during convalescence.

From this research it may be stated that ectropion is not erosion, nor is it eversion, nor is it ulceration. Erosion implies loss of tissue, so does ulceration, and eversion means the outward growth of the columnar epithelium to replace the squamous surface of the portio. What then is ectropion? Some of its attributes are well known. It is a circular, red, granular surface surrounding the external cervical os. It has no secretion of its own, but is usually bathed in cervical discharge. It bleeds readily if wiped with gauze or cotton and has a margin which is often difficult to define because it fades almost insensibly into the surrounding pearly portio vaginalis. It is always associated with a marked chronic endocervicitis, though not all cases of chronic endocervicitis are associated with ectropion. Chronic endocervicitis is a necessary antecedent to ectropion; and the ectropion is a sequel to chronic endocervicitis, if the latter is of long duration and of the proliferative type.

Ectropion begins as a chronic irritative microbic endocervicitis. It is found in virgins and in parous women. It is seen more commonly among the parous women because endocervicitis is so frequently a sequel of parturition. A close study of cases of chronic endocervicitis permits one to divide these cases into three great groups: first, those in which the microbic irritation tends to manifest itself in hypersecretion, as cervical leucorrhœa; secondly, those in which the microbic irritation produces hypertrophy and cervical polypi, and, thirdly, there may be cases when the irritation expresses itself in both hypersecretion and hypertrophy. Whether the infection will manifest itself in any one of the above ways will depend upon the attenuation of the microbe

and the reaction of the cervical tissues to that infection.

I have found that in virgins with marked cervical hypertrophy there is usually a constitutional tendency to hypertrophy of mucous membranes and adenoid tissue elsewhere in the body. The cervical mucosa in its pathology has a closely analogous parallel in the nasal mucous membrane. Now, the irritation of the cervical infection leads to determination of blood to that part—hyperæmia. That in turn, if long continued, leads to the development of new blood vessels, and that also in turn means over nutrition, which expresses itself in hypersecretion or hypertrophy. The processes of infection always begin in the delicate columnar mucous membrane of the cervical canal, which is more susceptible to infection than is the squamous covered portio vaginalis. But the squamous surface nearest the cervical canal cannot ignore indefinitely this vascular disturbance in its immediate neighbourhood. It soon feels the effect of the over-nutrition, and it feels it most in its deepest basal layer, which will begin to divide more rapidly, and, as the division speeds up, the superficial keratinized layers gradually fall off, and then division will be at the expense of differentiation. The superficial layers no longer have time to differentiate into squamous, keratinized, imbricated layers, but are pushed off and desquamated by the rapid division. Rapidly dividing cells have no time to become adult but remain in an embryonal state. So that ectropion is an area covered with embryonal squamous cells. Call it granulation tissue, if you will, but it is special granulation tissue which will revert if normal nutritional conditions and normal substratum are established.

The result is a slow spreading of the process from the cervical canal outwards and a gradual enlargement of the area of ectropion. It is in reality a skin disease, and simulates closely the changes that accompany acne rosacea, which, according to text-books on dermatology, begins as a hyperæmia, then follows the development of new blood vessels and is followed again by division of basal cells without proper differentiation. If we examine a number of cases of ectropion, we find that the outer border is ill defined, and you can actually see the pearly opalescence of the portio vaginalis being slowly lost, giving place to a bluish tinge due to underlying veins showing through the thinning squamous layers, and ending in the redness of granulation tissue. In other cases small arteries and veins break through and course centrifugally from the margin of the area of ectropion into the healthier distal parts of the portio. These vessels and their consequent hypernutrition are the forerunners of rapid division and lessened differentiation.

The clinical proofs of the above are to be found in the following statements. Try as you may, you cannot cure an ectropion without first or simultaneously curing the endocervicitis. The irritation of microbic endocervicitis is the primary cause of the ectropion, and the continuance of the irritation causes the ectropion to persist.

After cauterization of the cervical canal, not by deep incisions, but by careful superficial cauterization with a nasal cautery, followed by superficial radial cautery lines over the area of ectropion with a dull heat, a careful study of the regeneration of the tissue in the area of ectropion will prove interesting. A dull heat for the radial lines is to be desired because the only purpose one wishes to accomplish with this heat is to coagulate the underlying blood vessels which are promoting the hypernutrition. Dull heat is much more efficacious than red heat for that purpose. Dull heat may be applied for a longer period; it does not char, it penetrates more deeply, and it is a better coagulator.

The interesting sequel is that the squamous cells at the periphery do not grow in and cover the area of ectropion, as in any ulcer of the skin. No, you can actually see the reversion of the basal cells to their former type. They gradually lose their embryonal type and revert to the adult squamous type. This can be beautifully demonstrated by another method. First, cauterize the cervical canal with a dull-heated nasal cautery, to destroy its hypertrophied tissues and to coagulate its blood vessels. Then take the coagulation needle of the diathermia apparatus. Place one pole anywhere upon the patient and then plunge the coagulation needle about one-quarter of an inch into many spots in the area of ectropion. This effectually coagulates the underlying cervical blood vessels and the whole area of

ectropion gradually reverts, and in about four weeks has taken on the pearly whiteness of the normal portio vaginalis.

### CONCLUSIONS

Ectropion never exists without endocervicitis. Endocervicitis is a necessary antecedent to and is the causative agent of ectropion.

It is impossible to cure ectropion permanently without previously or simultaneously curing the endocervicitis. Incomplete cure of the endocervicitis will frequently be found to be the cause of disappointing results with cure of the associated ectropion.

Ectropion is a granular surface composed of embryonal squamous-celled granulation tissue.

This embryonal type of cell is the result of rapid division of basal cells consequent upon over-nutrition.

Removal of the causes of over-nutrition permits the basal cells to cease rapid division and allows differentiation and reversion to adult types to take place.

The best known means of accomplishing these objects will be found in dull heat for the destruction of hypertrophic tissues and for the coagulation and destruction of the new vascular channels.

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## DISABILITIES OF THE SHOULDER JOINT*

BY H. H. M. LYLE, M.D.,

*New York*

NUMEROUS articles have appeared in the medical literature on the subject of stiff and painful shoulders. Since the days of Duplay (1872), various etiological factors have been described, periarthritis, subdeltoid bursitis, partial rupture of the supraspinatus muscle, muscular strain of the tendons of the teres major or latissimus dorsi, birth trauma, brachial neuritis, unrecognizable subluxations of the humerus, lacerations of the axillary portions of the capsule, bruising of the cartilage of the joint, sprains of the deltoid, biceps and internal rotators. In shoulder joint injuries so many structures are involved that it is often impossible to identify the exact ones involved.

We shall not consider acute or chronic inflammation, osteoarthritic changes, or neurological lesions, but direct our attention to the treatment of traumatisms of the shoulder girdle that have resulted in pain, muscular weakness, and limitation of motion.

The shoulder joint is responsible for many clinical pitfalls. As a protection we insist on a careful x-ray study of every injured shoulder, no matter how slight the trauma.

### ANATOMICAL CONSIDERATIONS

When our ancestors walked on all fours the shoulder was a weight-bearing joint. In the process of evolution we have assumed the upright position, and the shoulder has become a hanging joint which must support the weight of the arm. The weight of the adult arm is 10 to 15 pounds. This weight is borne by four muscles; the biceps, triceps, coracobrachialis and deltoid. The capsule plays but a minor rôle.

Anatomically, the shoulder joint is a portion of the shoulder girdle. The peculiarity of this girdle, compared with the pelvic, is its mobility. This mobility is secured by the fact that the main attachments to the body are muscular. The only skeletal link is the clavicle.

The shoulder possesses the greatest range of movement of any joint. The mobility is made possible and enhanced by the fact that the shoulder joint is mounted on a movable base, the scapula.

The musculature of the joint consists of two half cones converging on the humerus. The infraspinatus, teres minor, and sub-scapularis converge on the head of the humerus; the lower half cone, consisting of the latissimus dorsi, teres major, and pectoralis major converges on the bicipital groove. The axis of this cone runs outward and slightly upward. In order to neutralize muscular cross tension and strike a physiological balance, the humerus

* Read at the Forty-ninth Annual Meeting of the Ontario Medical Association at Hamilton, on May 30, 1929.

is placed in this axis in the treatment of certain cases.

The inferior portion of the joint capsule is thin. When the arm hangs by the side this part of the capsule is thrown into folds. Between these folds adhesions may form. The synovial membrane of the joint presents three prolongations one down the bicipital groove, surrounding the head of the biceps; a second to the bursa of the subscapularis; a third to the bursa of the infraspinatus. Not infrequently, the sub-deltoid bursa communicates with the joint.

### PATHOLOGY

Trauma to the shoulder, judged by dispensary and insurance records, furnishes a high percentage of disability. The chief disabilities are stiffness and pain. Adhesions are the most frequent causes of these complaints. They result from incorrect treatment of acute bursitis, tendon strain, muscle rupture, bruised cartilage, fractures, dislocations, etc.

The shoulder joint, though seldom the seat of disease, is the joint most commonly incapacitated by adhesions. The trauma may be severe, often it is very mild; occasionally a history of trauma is lacking. After a slight wrench, exposure to cold, or during a light systemic infection, the patient complains that his shoulder is painful and the arm drags and nags. It becomes especially painful at night, and often wakes him when he turns. Pain at the insertion of the deltoid is common. Gradually it becomes increasingly difficult to abduct the arm. External rotation becomes restricted and painful. It is difficult and painful to fasten the back suspenders, shrug the shoulders, and button the collar at the back of the neck, but *forward motion of the arm persists after all other motions have disappeared.*

As the process progresses the arm is carried close to the side. Atrophy of the arm and shoulder muscles set in. The adaptive muscular shortening of the latissimus dorsi and pectoralis major, if unopposed, holds the arm in a position of adduction and internal rotation. This position favours the formation of adhesions in the capsule, in the peri-articular tendon sheaths, and the bursæ.

A painful joint which is rigid in all directions is the seat of arthritis. A painful joint which is rigid in certain directions, the other movements being normal, is free from arthritis, the limitations of motion being in this case due to adhesions and shortened muscles. The adhesions may be intra- or extra-articular. This classification requires modification when we deal with fractures into the joint with bony block, or with myositis ossificans of the surrounding muscles.

### TREATMENT

In the majority of cases, adhesions and muscular shortening are prevented by the intelligent treatment of acute and subacute lesions. A simple trauma of the shoulder can be turned into a real disability by acquiring the sling habit. The sling takes up some of the weight, but places the arm in a position of adduction and internal rotation. This is the ideal position for the formation of adhesions. It is also an active factor in producing adaptive muscular shortening. Disabling adhesions and shortened muscles encountered in the treatment of stiff and painful shoulders are often the direct result of the abuse of the sling. The disability may vary from complete ankylosis to a condition where pain is only elicited by some particular motion. For the present we will deal with the severe cases requiring manipulative treatment. A preliminary treatment of hot applications, massage, radiant heat, etc., is helpful but not a necessity.

A general anæsthetic (ether) is given to insure complete muscular relaxation. This is essential to the success of the treatment. Without an anæsthetic the patient will involuntarily put into action muscles for the protection of the joint, the adhesions will be incompletely broken, and a great risk is run of straining or rupturing the resisting muscles.

The movements are performed in a smooth, swift, and firm manner. All the movements of the joint are made, but not necessarily to the full extent of their range. The muscles have contracted in proportion to the limitation of motion imposed on them by the adhesions. The adhesions eliminated, treatment speedily restores the elasticity of the muscles. If a complete range of motion be sought at once irreparable damage may result.

After the adhesions are overcome, and while the patient is asleep, the arm should be placed in a position of full correction until he regains

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consciousness and is able to make a voluntary motion. The earlier the movement the better. The mental effect on a patient awakening and finding himself able to stretch is indeed striking. Rupture of typical adhesions is heard or felt, but if resistance is overcome by gradual stretching the prognosis is not so good. If this later condition is encountered the joint should be maintained in the correct position for a few days.

*Dangers.*—Fractures, dislocation, rupture of muscles.

Occasionally, full movement and freedom from pain follow the rupture of adhesions. This ideal result is rare. The mechanical obstruction is gone, but the muscles are so wasted and contracted from disuse that they are physically incapable of normal work. Merely ordering the joint to be used is useless. Few people have the will necessary to make muscles perform in the presence of pain. In such cases the use of graduated weights and pulleys is valuable. By persisting, the patient soon learns that with the increase in strength and mobility the pain decreases.

Exercises are to be diligently persevered in until the muscles regain their former bulk, and the joint its full power of movement. John Hunter, the famous surgeon, said: "The power to heal is the property of living tissue, but the power to recover function is the property of the patient's will and brain." The surgeon's duty is to direct, encourage and interest the will and the brain.

SUMMARY

1. A common cause of shoulder disability is the presence of fibrous adhesions and atrophied muscles.

2. Adhesions and atrophy should be prevented by the physiological treatment of the acute traumatic lesions.

3. If the adhesions have resisted the ordinary therapeutic measures they should be broken up under ether anæsthesia.

4. Free motion of joint should be sought, but a complete range should not be tried for at the expense of damage to the contracted muscle.

5. No case should be dismissed from the care of a surgeon until the muscles of the joint have regained their normal bulk, and the joint has its full power of motion.

## THE CLINICAL SIGNIFICANCE OF SOME TRENDS IN ADOLESCENCE*

BY W. T. B. MITCHELL, M.D.,

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THE psychiatrist in a large part of his clinical work among adults is faced with the realization that he is dealing constantly with deeply seated personality disturbances which have had their beginnings far back in the individual's developmental history. It seems reasonable to believe that the earlier in development we attempt to treat overt trends the better the results of treatment. I think that the studies of behaviour disturbances in the adolescent period support this view and at the same time give us definite leads for constructive work in the mental health field in the pre-adolescent periods of development. It is important that the general practitioner and internist should recognize the significance of some of the deviations from healthy normal mental development and realize something of the possibilities for treatment. The disturbances of the adolescent period bear an obvious relationship to adult psychiatric problems; hence the attempt in this paper to deal briefly with some of the situations occurring during this period of growth and development.

The period of adolescence—the period between childhood and adulthood—a transition period—a period of physical and emotional maturing—a period in which the individual for the first time is completely conscious of himself in re-

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lationship to his fellows and in relationship to the universe—a period of independent effort when normally a part of the emotional dependence on the home situation is wiped out and new and compelling emotional relationships are set up outside the family—all of these changes tax the individual powers of adjustment and make for behaviour situations which adults frequently fail to understand. The unwise handling and, on the other hand, the ignoring of significant developmental trends in adolescence are unquestionably responsible for many situations in adult life which are of frank significance from a psychiatric standpoint, and for many more which are significant from social and economic standpoints. The social aspects of the problem are as important to the mental hygienist and psychiatrist as are the frankly medical aspects. Statistical studies indicate the expectation that one person out of 22 in one generation will in the course of his lifetime suffer from grave mental disease. It is not possible to state definitely the expectancy for the more or less serious lacks of adjustment which interfere with social and economic success. The writer does not believe that it is possible to differentiate completely between the failure of adjustment which is marked by a psychoneurotic development, by a psychotic episode, or by a progressive and continuous mental deterioration, and the failures of adjustment which are marked by the less dramatic social and economic failures. How much of actual mental disease may be prevented by a consideration of the problems of adjustment during the developmental period is open to question. Observations all along the scale would seem to make this one of the most hopeful fields of medical practice. The same set of observations point to the possibilities of a constructive effort on the social side that will be worth-while.

From infancy to puberty there is normally a progressive turning of the child's interest from himself to outside people, things and activities. In this period, particularly at the ages of two and three years, we see transitory evidences of the child's self-interest in such manifestations as thumb-sucking, masturbation, etc. Occasionally, where these manifestations have not been accepted for what they are, *i.e.*, transitory things in the process of the turning-out of the child's interest, and where unwise methods have been used, we see later in this period the continuation of what we may think of as infantile responses, *e.g.*, enuresis, thumb-sucking, masturbation, etc. One of the major objectives during the pre-adolescent periods should be the providing of settings which will place no obstacles in the way of this progressive turning-out process. (By the time a child is ten or eleven years of age the broader the spread of interest and energy the better from the standpoint of successful adjustment during the adolescent period. Anything which has succeeded in seriously throwing the child's attention and energy back to himself is unfortunate and frequently prolongs the period of in-turning which is inevitable at the time of puberty.)

The early adolescent period is marked by the appearance of sensations and feelings new and disturbing to the individual. There are the signs of physical maturing—a change in the growth curve, the appearance of the secondary sex characteristics, the growth and development of the sex organs, the appearance of spermatozoa in the sexual secretions, and of menstruation, etc. In the boy the automatic and frequent erections, and the appearance of nocturnal emissions, provide sensations at once new and frequently disturbing—disturbing particularly where previous teaching and training have been responsible for the building-up of attitudes which have put sex apart from other functions and have established all things related to sex as wrong or sinful or shameful. All of these changes occurring at puberty inevitably throw the child's interest and energy back to himself. The energy which has previously been devoted to school work, gang associations, games, etc., is partially withdrawn. The boy or girl is sensitive, shy, self-conscious. There is frequently an apparent slump in school performance and in performance apart from school work which appears quite unreasonable to teachers and parents, who fail to realize that the young adolescent is passing through a very difficult period of re-orientation. He takes personally the sarcastic general references of the irritated or facetious school master, sometimes with serious rather far-reaching results in his later personality organization. Normally, this period or phase of self-interest is followed by evidences that the individual's interest is once more being directed to outside things—to social interests, to play, to emotional attachments

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directed first to individuals of the same sex, later to individuals of the opposite sex, and also to vocational interests. This normal progression is evidence of a satisfactory adjustment. Where we fail to find this progression, but observe an undue prolongation of the behaviour which normally characterizes the early adolescent, we are justified in believing that the individual is experiencing difficulties in satisfactorily orienting himself in the new conditions set up by puberty.

Perhaps the three most serious conditions to which the adolescent must adjust himself are: (1) his experiences related to sex feelings; (2) his social relationships; (3) his urge towards independence. In the clinical field these three conditions cannot be considered apart from one another, since they are all three so closely interrelated.

As I have suggested previously, we succeed rather completely, by our conventional attitude towards sex and our inability to completely integrate it with other functions, in building up in children an attitude which in adolescence makes for fear of personal sex experiences. The child's curiosity and interest are directed to his own sex feelings; the censor indicates that these things are outside normally acceptable experiences. Thus the situation is already made for a tremendous conflict. The child so faced must either reject and repress completely his natural interest in his own sex feelings, or he must accept this interest, with which all his previous experience has placed him in conflict. In the first instance the conflict gradually assumes a place outside consciousness and is replaced by compensatory behaviour, which on the surface appears quite unrelated. In the second instance the conflict continues on a conscious level and with an undue continuation of the period of self-consciousness, marked by sensitiveness, seclusive behaviour, with failure in making the normal, social, and play, and later heterosexual contacts of the period.

### CASE 1

To illustrate psychoneurotic development following the rejection from consciousness of the natural instinctive self interest.

A girl, 23 years of age, referred for examination because of compulsive feelings and fears. She had a constant fear of pins and needles and sharp pieces of glass, and at the same time a compulsion to touch or interfere with such objects as a glass showcase, a pin basket, an iron rod under the seat of a railway carriage, a man-hole cover, etc.

Between the ages of nine and twelve years she had engaged in some sex practices with a school girl her own age. The patient herself was an only child. At the age of twelve she was troubled by the situation and discussed it with her mother. The mother was shocked, and her attitude served to increase the child's fear of the situation. From that time the girl shut out completely all homo-sexual and auto-erotic practices and all thoughts of sex things. During the early adolescent years, and particularly at night, there was a fear of sharp splinters of glass. She recalls the constant fear in drinking a glass of water at bedtime that there might be a splinter of glass. She would drain the glass lest a splinter would do harm to someone other than herself. She was regarded by relatives and friends as a girl of extremely high standards. Her general conduct was held up to others as a model. She was most scrupulous regarding personal cleanliness, and had a more or less constant fear that her clothes might be handled or worn by other girls. She always locked her room door and trunk when away from home to avoid such an occurrence. She accepted these feelings as perfectly natural, as did her friends. She did not form close friendships, feeling always that her standards and interests were somewhat above those of the group.

A few months before being referred for examination there had been an emotional crisis in the form of an engagement and shortly after this incident there developed in an acute way the fears and compulsive feelings referred to in the complaint. The symptoms were seriously inconveniencing. After any sort of expedition, several times during the day, she and her friends would search painstakingly through her clothing for concealed pins, etc. The mechanism of development as revealed in the course of treatment seems to be fairly clear. A sex situation which in the pre-adolescent period was accepted without much feeling—the adolescent conflict—the repression of the conflict out of consciousness—the substituted fears and other compensatory behaviour—the emotional situation in early adult life which revived in an acute way all the psychoneurotic symptoms. Under treatment, the patient was able to accept the sex situation at a more adequate adult level. This patient was treated while still in the late adolescent period. The ultimate results of treatment are doubtful. There was, however, the willingness and ability to accept the marriage situation and the disappearance of the more acute symptoms.

Psychiatrists are familiar with the extreme difficulty of dealing with such "psychasthenic reaction types" in more advanced periods of life. I think I recall hearing someone say "Once a psychasthenic always a psychasthenic." Such a statement is open very distinctly to question in the light of a better understanding of the mechanism of development and if we are impressed with the importance of dealing adequately with such situations in the early adolescent period. The ideal time for treating such a problem may be illustrated by the following brief case history:

CASE 2

A boy, 13 years of age, referred for examination because of a change in his general behaviour in the past six months. Prior to this time he had been jolly and care-free, with adequate social and play interests. Now he was staying by himself and apparently greatly concerned about being able to do simple things, such as opening a door, and, particularly, about telling the exact truth. He was concerned about certain instances in the past—as to whether he had paid back a car ticket borrowed several years ago, etc. While the content is slightly different from that of the first case described, the indecision was the most marked characteristic, the boy never being able to make up his mind that any task was finished. In making an answer to any direct question he would always leave himself a loop-hole by saying "or" in an inaudible tone. Here again we have a picture which, with remarkably little change in content, would make a fitting chapter in the life history of the previous case. The appearance of the symptoms seem to be related to a class-room lecture, the occasion for which was the discovery of some obscene note. The lecturer's major note, needless to say, with all of the lack of understanding which prevails in our traditional educational institutions, was one of warning—its result, the precipitation of the instinctive conflict in this thirteen year old patient. From the treatment aspect everything suggests a satisfactory re-adjustment—in the resumption of social and play interests and a gradual disappearance of the lack of confidence and indecision.

The whole question of the treatment approach to the problem at this age level cannot well be included in this paper; that, together with the results of continuous observation during the adolescent period, may later be reported.

I would like to report a case with marked anxiety feelings, reported previously to the Ontario Neuro-Psychiatric Association in May, 1927.

CASE 3

A boy of 14 years was referred for examination because in the past six months he had had periods in which he complained of weakness, pains in his heart. He feared he was dying and created a scene. The parents were fearful that there was something the matter with his heart and that these attacks might have a serious result. He experienced these sensations both day and night. He had also developed a tic-like movement of the head and occasional tremors of hands and legs.

In the history one notes that in this home the parents for many years have placed perhaps an undue emphasis on health subjects. They have collected all sorts of health literature. The father takes his systematic daily exercise very seriously. The mother is an over-conscientious, extremely sensitive, woman, much attached to and concerned about the subject, who is the eldest of three boys. In the boy's history we find that between the years of eight and eleven he had a cough, for which he was repeatedly examined and treated by several physicians. Finally, it was suggested that the cough was simply a nervous manifestation. It disappeared completely two years before he came to see us. Physical examination was essentially negative. His intelligence was adequate, but on the emotional side we observed an extremely anxious, hypochondriacal youngster. At the first interview it was evident that he was consumed with curiosity about sex questions; for the past six months he had been definitely faced in his own mind with the question of what would happen if he were to masturbate. He read in a book that this was a very harmful practice and to be avoided absolutely. He asked elsewhere and was warned never to yield to his impulse, for masturbation was harmful to the body and might lead to insanity. He had this constant curiosity to know the why of things—the impulse to satisfy his curiosity. At the same time he was strongly inhibited by the fear produced by the warnings he had received. The conflict which resulted was enormous and resulted in the very marked anxiety condition in which we saw him. The attitude of the psychiatrist, who regarded all of this boy's curiosity and all of his feelings as perfectly natural, was quite beyond the youth's comprehension, in the face of the fact that his previous questions had met with such a concerned serious response. In May, 1927, I reported that "the anxiety-symptoms have disappeared. The mother and father have been able to take a much more healthy attitude to the whole situation."

Here we have a situation which from a clinical standpoint is not essentially different from the full-blown anxiety states which one may meet in a mental hospital. The influence of the environmental factors would seem obvious, and the effects gained from a correction of these factors equally evident. In the summer of 1927 there was some brief recurrence of the anxiety symptoms; for the past two years they have been completely absent. The boy has at the same time shown every evidence of making a satisfactory adjustment in the home, school, and social situations.

CASE 4

To illustrate development of psychotic symptoms following the continuous instinctive conflict on a conscious level throughout the adolescent period:

A male, 24 years of age; occupation, secretarial, (had had very satisfactory advancement). He was referred for examination in October, 1927, for a psychotic episode. He stated that he was "Christ"—that he would reveal himself to the world in the ensuing week. There follows an excerpt from a letter written by this patient:

"I feel that the time has arrived when I should furnish you, in concrete form, an outline of the events leading up to my conversation with you in your office on the 28th of October, as well as subsequent developments.

"As regards the first twenty-five years of my life, they were spent (outwardly, at least) in very much the same manner as that of thousands of other youths. Inwardly, however, I feel there was a great deal of dissimilitude as between myself and the thousands of other people I speak about. I was frequently subject to nightmares and more than occasionally heard very loud knocks proceeding from various articles of furniture in my home. I also distinctly recall having been greatly troubled, when about ten, as to the destiny of my soul; the result of my thoughts was to decide that when I felt my end was near, to hire several soldiers to stand guard over my body, so that neither angels nor devils could detach my soul from it when death came.

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As I have already informed you, it is my belief that the period from Sunday, October 22nd to Sunday the 29th, 1927, bears a connection with Easter Week. It was made known to me late Saturday evening, the 28th, in a way which I cannot at present explain, that I was singled out to complete the work started by Christ while He was on earth, *i.e.*, to eventually bring all the inhabitants of this earth to the True Faith. The eight days of which I speak were, save for Friday, remarkably bright ones, and whenever I appeared on the street the sun shone with great brilliance. Another extraordinary thing is that a white light of supernatural brightness frequently proceeded from my eyes, and but very few people were able to look at my eyes for more than a second or two. This has since disappeared.

I next discovered that animals of all sorts were very much afraid of me and averted their eyes whenever I looked in their direction. This supernatural quality (if it may be so termed) has also left me, but has been replaced by the power of making animals exceedingly docile by simply looking at them for a few seconds. The power of hypnotism has, to a certain extent, been infused in me, and I feel that with a little development it will be possible to expand it to considerable proportions.

Then, too, most of my thoughts seem to be instantaneously transferred to the minds of other people; should I hum a tune in my mind those around me listen in a rapt manner and by raising my *mental* voice, those within three hundred feet or so of me distinctly hear what I am saying internally; however, this does not apply in the case of persons engaged in conversation or who have their minds concentrated on the reading of a newspaper, etc.

You, of course, have taken note of the remarkable series of happenings this year—for instance, the Mississippi flood, the movement of a volcanic island lying off Alaska approximately four miles, the unusual fall and early winter weather which, in many instances, resulted in a third crop being harvested and roses growing in Ottawa, etc. Vast regions have been laid waste, but Canada (and especially the Province of Quebec) has gone almost untouched. It is my belief, in this connection, that Almighty God is pleased with this young country and particularly with its metropolis, Montreal. Churches are to be seen on all sides and there is a distinct feeling of reverence in the hearts of many Montrealers, as well as residents of other portions of the Province of Quebec.''

*History.*—One of three children; an uneventful childhood. He had had a marked conflict over sex problems throughout the adolescent period; the religious side of the conflict, marked. Continuance of auto-erotic practices into late adolescent period. Brief periods of depression which did not interfere with his work, but during which, over a period of two or three weeks, work appeared more difficult. At the age of 24, the psychotic episode referred to in the complaint. Result: apparent recovery, with apparently a good deal of insight. Uninterrupted work during past year.

I wonder if it requires too much temerity, in the light of information revealed during the treatment period, to say that we have been dealing here with a problem which had been unnecessary if the earlier adolescent conflict had been adequately dealt with.

### CASE 5

To illustrate the more opportune time for the initiation of treatment, with the possibility of preventing frank psychiatric development. This boy's behaviour was such as to alarm his family and to suggest possible overt mental development to the referring physician:

A male, aged 18 years, showing a very marked over-activity in general behaviour; difficulty in carrying through any consistent plan of work; disturbed sleep.

*History.*—He was the youngest in a family of four, separated in age by 14 years from the next oldest; very dependent and self-assertive during the pre-adolescent period. He evidenced marked sex conflict, continuing auto-erotic practices, religious conversion, fear of insanity, etc. There was here no actual psychoneurotic of psychotic problem, but a situation pregnant with possibilities. Under treatment he appears to have made a satisfactory adjustment, with a good deal of insight.

Aside entirely from conflict over sex questions, the individual may find it difficult to establish social contacts. He experiences the feeling that all of the new experiences of which he is conscious sets him apart from other people. He is for the first time in his life intensely conscious of himself as an entity; he is living for the time being in a state of comparatve isolation in which ideas of reference and a consciousness of individual differences assume very large proportions. He may rationalize the feeling that he is not welcome or wanted by companions by obviously avoiding such contacts and attaching himself conspicuously to older individuals, or devoting himself rather exclusively to some particular work. He frequently fills up the gap in such a relationship by an inordinate amount of day-dreaming, in which he compels the attention of his contemporaries.

### CASE 6

To illustrate psychotic development which appears to have emerged directly out of adolescent social conflict.

A male, aged 18 years. *Complaint*: In the past few months he had shown an indifference to his personal appearance. In last three weeks he had spoken of teachers following him, controlling his actions and thoughts. The family had noticed him walking about, laughing without apparent cause, etc. Two of his letters follow.

''Dear Miss Smith:

''This is in answer to your 'dare'. I am absolutely sure that you and Mr. Brown are constantly following me and have been doing so since I was about four or five years of age. I am sure that you can make yourself, and others, invisible to me, untouchable, and inaudible. I am sure that you live right upstairs at 365 Young Street. I am sure that you and Mr. Brown can hear my thoughts. I am sure that I am sane and that, although you and Mr. Brown have for the last few days been invisible to me, you are still constantly watching me. I hope that this will make you as sure of my being certain about this as I am sure about all.''

"Dear Miss Smith:

"After careful consideration on my part, my opinion is just the same. I am *absolutely* sure that you and your husband, Mr. Brown, have been following me since I was about four or five years of age and are still constantly watching me. I am also sure that I am as sane as anybody else and that you believe me to be sane, although you are trying to make me think otherwise, in order that I should give up the idea that you are following me. A proof is a proof; even when Miss Smith, and Mr. Brown, and Mr. Green say that it is false, it is still true. I have *proved* it so to my satisfaction.

"If you will stop pretending you are not watching me, then I will get down to seriousness in my school work. JOHN."

Since early adolescence the family observed the patient to have become more and more seclusive and studious. During these years he was concerned over his failure to make friends; he persuaded himself that he did not care for companionship and would devote himself to science. He day-dreamed a great deal. In his dreams he always pictured himself as someone "important", as having made a great discovery which would attract the attention of the world and which would be used for the benefit of humanity. It seems just one logical step further in the release from an unpleasant reality to pass along from the day dream, where the relationship of the dream to reality was recognized by the subject, to a fantasy formation, which had to the subject all the appearance of reality. No psychiatrist would question the ominous appearance of this picture arising, without much question, as a direct resultant of the adolescent conflict. The patient is back in the school situation. The ultimate outlook is doubtful. The importance of having attempted to deal with the problem at an earlier level is obvious.

The third type of conflict may arise over the ego urge to independence, especially in cases where an undue dependence has been built up around the family situation. The solution which has previously proved satisfactory to the individual, *i.e.*, the evasion of unpleasant and difficult situations by falling back on the family situation and usually on a single member of the family—the mother or the father, or a substitute for either—no longer is satisfying in the face of the counter urge towards independence. The resulting conflict may result in a fixation in the emotional maturing instead of the normal healthy progression referred to previously.

## SUMMARY

1. The period of adolescence presents many difficulties to normal healthy emotional adjustment.

2. Many situations arise during this period which are significant from psychiatric and social standpoints.

3. Conflicts arise chiefly around: experiences related to sex feelings; social relationships; the urge towards independence.

4. It is reasonable to believe, in the light of clinical experience, that individuals may be satisfactorily tided over many difficult situations in the adolescent period, and that a certain proportion of adult mental disease may be averted; that, at the same time, there may be prevented many later individual social problems.

5. It is important that we should have a more widespread understanding of adolescent problems on the part of parents, teachers, and physicians.

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A NEW LOCAL ANÆSTHETIC—H. Flörcken and O. Mues describe the uses of a local anæsthetic of a complicated derivative of the quinoline series, to which also belong a number of other useful medicinal products such as atophan and yatren. This substance, which is marketed under the name of "perkain," forms colourless crystals which are readily soluble in water with neutral reaction, and which, unlike cocaine, can be sterilized by boiling. It should be kept in alkali-free glass vessels, and to ensure this it is recommended to add a few drops of dilute hydrochloric acid to each litre of the solution. The local anæsthetic action of perkain is said to be far greater than that of cocaine—as much as 100 times greater when applied to the rabbit's cornea; perkain 1 in 1,000, acting for one second, has about the same effect as 1 in 1,000 cocaine acting for half a minute, as estimated by the acid stimulant effect on the nerve endings of the reflex frog; the drug is, however, about five times more poisonous than cocaine, and deaths are recorded from doses of 0.13 and 0.2 gram of the substance. It is chiefly recommended for its slow rate of elimination and more prolonged period of action, which may extend to several hours; the after-pain is said to be much less than after novocain. The maximum dose has not yet been determined, and it is advised that the drug should not be used in concentrations of over 0.5 to 1 per 1,000—*Münch. med. Woch.*, p. 1714, October 11, 1929.

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# THE INDICATIONS FOR THE USE OF INSULIN*

BY WALTER R. CAMPBELL, M.A., M.D.,

*Toronto*

THE treatment of diabetes mellitus must always include the education of the patient in the selection of a suitable diet, but since 1922 the rigors of the dietetic regimen have been much reduced for many sufferers from this disease by the introduction of insulin. In addition, insulin has made possible the successful treatment of many diabetics whose condition was not amenable to former methods of treatment. The economic value of lives and suffering saved by this discovery is now well nigh incalculable.

Insulin, the active hormone of the pancreas controlling carbohydrate metabolism, is produced in Canada by the Connaught Laboratories of the University of Toronto, in 10 c.c. vials of four strengths: 10, 20, 40 and 80 units per cubic centimetre. A unit of insulin is now defined by the Permanent Standards Committee of the Health Section of the League of Nations as equivalent to the effect of one-eighth of a milligram of a certain preparation of dry insulin hydrochloride. This value is, for practical purposes, identical with the earlier Toronto clinical unit, and under suitable conditions is capable of providing for the utilization of 1 to 2.5 grams of carbohydrate in man. It should be remarked that this standard preparation is not pure insulin. Crystalline insulin, which appears to be a chemical entity, has been prepared by several workers. It is about three times as active as the standard powder. Despite the unwarranted claims of certain manufacturers of gland extracts, insulin is destroyed in the gastro-intestinal tract. It must, therefore, be administered hypodermically, and, as a rule, within the half hour preceding meals. The duration of its effect may be taken as six to eight hours, and rarely twelve hours, hence the need for repeated injection. Most of the insulin used in Canada is made from beef pancreas, but for those who are sensitized to beef protein insulin from pork pancreas is available.

The question, Who needs insulin? is in some degree dependent on our ideals in the treatment of the diabetic patient. Short of the cure of diabetes, which neither insulin nor any other known remedial measure will induce, I believe the therapeutic aim in diabetes should be: (1) provision of adequate rest to the damaged organ, the pancreas; (2) provision of a supply of food adequate to carry on the body processes and to restore the patient to a state in which he can regain earning power.

Consideration of these principles of treatment will develop groups of diabetics who need insulin temporarily or permanently. For convenience, they may be arranged as follows: (1) the acidosis cases; (2) the coma cases; (3) the infection cases; (4) the pre-operative cases; (5) the low carbohydrate tolerance cases. The greatest mortality of diabetics comes in the first year after the discovery of the disease. For this the first three groups are very largely responsible, and it is here that the most dramatic effects of insulin are observed. It is true that the acidosis of diabetes can usually be controlled by dietetic measures alone, but often these patients pass almost imperceptibly into coma from which it is more difficult to rescue them.

## ACIDOSIS

With adequate treatment no case of acidosis need go into coma and in case of doubt it is best to use insulin, even unnecessarily, rather than run undue risks. An excess of insulin in these cases is avoided by coincident administration of glucose or other carbohydrate, in the proportion of one gram for each unit of insulin given. The indications for insulin are the presence of acetoacetic acid in the urine, as determined by the ferric chloride test, with signs and symptoms of acidosis and dehydration, such as deep breathing, which may be

* Read at the annual meeting of the Ontario Medical Association, Hamilton, May 30, 1929.

prolonged, painful or laboured, often nausea, vomiting and abdominal pain, vertigo and a fruity odour on the breath. Drowsiness appears and gradually becomes more marked while one may be misled by the marked anxiety, restlessness, and delirium which sometimes occur. If the skin and tongue are dry and hard and the tension of the eyeball is reduced the patient is in imminent danger of coma and the treatment should be vigorous.

The patient should be put to bed, kept warm, and encouraged to rest. Morphia is seldom indicated on account of the complicating factors it introduces. Warm drinks of all kinds should be provided liberally and the patient must be continually urged to accept them. A cleansing enema is often useful. The most important part of the treatment, however, is insulin, 20 to 40 units, accompanied by a drink of orange juice, grape juice or diluted corn syrup, given as an initial dose and repeated every three to four hours until the symptoms disappear. Repeated examination of the urine to make sure that glycosuria persists will prevent any tendency to hypoglycæmia.

Forty units of insulin per day, in divided doses, will keep most cases out of danger until the diet and insulin can be more suitably adjusted. On the days immediately following an acidosis the type of food most acceptable to the patient may be used and strict diet introduced gradually as recovery ensues. The use of sodium bicarbonate during the period of acidosis is hardly necessary, but 10 grams (150 grains) given by mouth does no harm and, in my opinion, accelerates the recovery.

### COMA

Next let me repeat what has been said elsewhere: save for infection, coma is due to carelessness, usually on the part of the patient. All acidosis cases can be improved; not all comas can be cured. Coma is an emergency and must be treated as such. The loss of one hour is an inexcusable delay and the price is often the patient's life. There cannot be the slightest doubt that insulin for emergency use, like other biological preparations, should be readily available, no further distant than the office of the nearest Medical Health Officer. Coma is best treated in hospital, but most cases could be saved by an initial dose of 60 units of insulin on diagnosis. If possible the patient should be made to take 2 to 3 ounces of corn syrup, diluted with water or coffee, by mouth. Many times this can be swallowed when the patient appears completely comatose.

I shall not dwell on the differential diagnosis of coma, but merely point out the possibility of coma, even in diabetics, being due to another cause. This, however, is impossible if acetone is present on the breath, except perhaps in children. Children, in this connection, also present another unusual condition; in them a diabetic coma may develop without dehydration. Dehydration of some degree is, however, the rule in adults passing into diabetic coma, and probably contributes much to the severity of the condition. In the treatment of advanced coma it is necessary to use not only insulin, the most important drug, but also to rectify the other abnormalities occurring. Cessation of ketone production should be induced by adequate provision of the calories required in foods other than fat. The metabolism should be reduced to the minimum by putting the patient to bed and keeping him warm. One hundred units of insulin, with 1,000 cubic centimetres of 10 per cent glucose solution, are given intravenously as soon as possible. Further doses of insulin and fluid may be given if necessary, but seldom are the subsequent doses so large. Perhaps 200 units in all are sufficient to overcome the coma completely. Larger amounts may be given, if necessary, provided care is taken to balance the insulin given by adequate amounts of carbohydrate. I prefer to have the patient excreting sugar in the urine until he is able to take an interest in his condition again. Further fluid administration will be required, but usually this can be given by mouth. An unknown quantity of insulin will be necessary to prevent relapse into acidosis as the patient is gradually introduced to more and more solid foods, but two doses per day of twenty units each will be found sufficient at first and the more accurate adjustment of dosage can be made as the evidence of its need accumulates. During the comatose state 15 to 20 grams of sodium bicarbonate, or its equivalent, may be given in divided doses. I have never known of any deleterious effects from such doses, and am convinced of their value in producing a more

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rapid relief of the patient. Circulatory support is sometimes needed and for this purpose one-quarter c.c. of pituitrin or pitressin may be repeatedly administered intravenously.

### INFECTIONS

The diabetic with infection is a much more serious problem than the ordinary case. If free drainage of pus can be established it should be done immediately. If, as in pneumonia, this cannot be accomplished the patient must receive the treatment indicated for his condition. His caloric intake should be increased above that ordinarily required at rest and, as a rule, the bulk of the food should be decreased. Many times it may be desirable to resort to milk, cream, and egg mixtures, with orange juice. For some unknown reason much more insulin than usual is required to control acidosis and glycosuria during infections, but care must be taken during the period of recovery to avoid hypoglycæmia from overdosage. While one should attempt to balance the patient's diet and insulin to maintain the urine sugar free and his blood sugar approximately normal, at times this cannot be accomplished. Such patients should be given sufficient insulin to prevent acidosis and, if necessary, orange juice or other carbohydrate given to avoid hypoglycæmia. It is also useful to cut down the size and increase the number of doses used. The older view that glycosuria or high blood sugar *per se* prevented healing is undoubtedly incorrect, but it is quite true that a normal metabolism of the cells under the influence of sufficient insulin materially assists in the repair of the injury.

### PRE-OPERATIVE CASES

The diabetic requiring operation often needs additional insulin as a safeguard against post-operative acidosis. Needless to say chloroform, which damages the liver, should never be used as the anæsthetic in these cases and ether as little as possible. The operation should be performed under spinal anæsthesia, para-vertebral nerve block, or gas and oxygen, if possible. No purgatives should be employed, but an enema should be administered if necessary and, as a rule, morphine or morphine-scopolamine should be used as a preliminary to the anæsthetic. I do not feel that, given adequate preparation, the metabolism of the diabetic imposes any greater risk than another surgical case of the same sort. It must be admitted, however, that some organic changes associated with the diabetes increase the surgical risk to a degree comparable with that of a non-diabetic individual some ten to twenty years older. For this reason one does not favour the operative treatment of readily controllable hernias in elderly diabetics or operations of like nature. Preferably a week or more can be profitably spent in preparing a diabetic for operation, the amount of preparation and the amount of insulin used varying of course with the case. In cases of emergency the patient may be given a glass of orange juice by mouth previous to operation, or if vomiting 25 grams of glucose in 50 per cent solution intravenously and 25 units of insulin, and post-operatively treated as a possible case of acidosis. In the average case the patient should be given a glass of orange juice to drink three hours before operation and be instructed to lie on his right side. The orange juice should be repeated two hours before operation. With each glass of orange juice 15 units of insulin should be given subcutaneously. Post-operatively the patient should be replaced on a diabetic diet as soon as possible, but if there is much delay before he feels able to take food the pre-operative treatment should be repeated at intervals of three to four hours in order to prevent the development of an acidosis. In the milder cases of diabetes insulin treatment is not imperative in preparation for operation nor as a post-operative measure. The frequent temporary fall in carbohydrate tolerance after operation, however, makes it desirable as a protective measure in all but the mildest cases. In these the same effect can be secured by a considerable reduction in the carbohydrate intake for three or four weeks after operation. Both insulin and dietary reduction for some weeks may be desirable in the more severe cases.

### LOW CARBOHYDRATE TOLERANCE CASES

Notwithstanding its great importance in the foregoing types of cases the most important indication for insulin is in those cases of diabetes with low carbohydrate tolerance. In the more or less temporary phases of maximal

insulin deficiency it is life-saving. In the low carbohydrate tolerance cases it not only prevents the development of the acutely fatal condition of diabetic coma but it enables the individual to recover his strength and regain his earning power, and this is important not only to the patient but also to the material welfare of his family.

Adequate control of the intake of food is a fundamental basis for the use of insulin in diabetes. No patient should receive insulin on anything but a weighed diet suitably constituted to fulfil his caloric requirements. Many plans of satisfying these requirements have been adopted by different workers. Naturally, these are not without their good points, but for satisfactory treatment over long periods of time we prefer a method which has been previously described. Insulin will make any plan or no plan work for a time.

When a patient can metabolize a suitable diet without insulin there seems to be little use in prescribing it. Nevertheless, patients have often been given insulin in considerable amounts immediately on diagnosis and such treatment continued until dangerous reactions compelled its cessation, when it was found that the patient did not need it. This does not indicate improvement in tolerance, as is sometimes stated, but merely a mistake in estimating the severity of the case. True improvement in tolerance is very slow to develop. On the whole it seems better to study the behaviour of the patient on a known diet equal to his basal caloric requirement and prescribe insulin if and when needed. Insulin is needed when the patient does not become aglycosuric or attain a normal blood sugar level within a few days after commencing treatment. The average glucose excretion in grams per twenty-four hours divided by 1.5 gives the amount of insulin required to make him sugar free. An increase in diet approximating 50 per cent of his basal caloric requirement will be necessary in order to return the man to work. This is best made by gradual additions to the diet over a period of two to three weeks. More insulin may be necessary to prevent hyperglycæmia and glycosuria. The total glucose value of the dietary increase divided by 1.5 gives a measure of the additional amount of insulin to use. Before discharge the patient's blood sugar should be brought to normal on his maintenance diet. Two-tenths of the excess blood sugar level (over 100 mg. per 100 c.c.) gives the number of units usually necessary to accomplish this. Needless to say, the patient taking insulin requires additional training as compared to the patient on diet alone. He should be taught to sterilize syringes and needles, measure and inject his insulin, and to recognize and cure hypoglycæmia, in addition to the training in the nature and course of the disease, diabetic dietetics, and the urinalysis required by the milder type of diabetics.

### ANOREXIA

Perhaps one should not omit from this discussion the indications for insulin in non-diabetic cases. Among the thousands of papers now written on insulin there are some recommending it on quite insufficient grounds for almost every ill to which flesh is heir. As might be expected these enthusiastic reports have remained unconfirmed by later work and insulin is still used in the main for its specific effect on metabolism in diabetes. Occasionally, it can be made to serve another purpose however. One of the early symptoms of insulin over-dosage is hunger. In intractable anorexia from various causes hunger may still be induced with insulin when other measures completely fail. Beginning with doses of 10 units, increasing amounts of insulin are given until a hypoglycæmia is induced and hunger experienced, when the food chosen by the patient is supplied to him. Increasing amounts of food at meal times with sugar-containing drinks between meals are allowed, care being taken to retain the hunger sensation by adequate increases in the dose of insulin. The bowels should be carefully regulated and, in convalescence from acute illness or the other cases where anacidity may play a rôle, ac. hydrochlor. dil. may be used. Tonic mixtures, hæmatinics, and graduated exercise may also be employed. With a little care a daily intake of 4,000 to 5,000 calories is readily attained, with a considerable improvement in the asthenic state of the patient. The ultimate prognosis is of course dependent on the nature of the condition underlying the anorexia.

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### THE DANGERS OF INSULIN

The most readily apparent danger is that of an overdose producing hypoglycæmia, or excessive lowering of the blood sugar. It may occur if heavy doses required to cure acidosis or coma are long continued, if the natural tolerance increases, if over-exercise is indulged in, or the insulin is administered without its balancing dose of food, as for example, when the meal is long delayed, the patient vomits, has diarrhœa, or delayed digestion of his food from any cause.

The symptoms which the patient experiences are sudden pronounced hunger, weakness, fatigue, tremulousness with pallor or flushing of the face, dilatation of the pupils, and, in children, increase in the pulse rate. Sweating, tremor, and inco-ordination of the muscles follow, and the vague feeling of inquietude becomes a definite anxiety, with various forms of emotional upset. Various forms of mental unbalance, aphasia, disorientation, delirium and confusion follow, to be succeeded by collapse, unconsciousness, and death, unless suitable treatment is undertaken. Fortunately, the cure is easy and specific. While there may be some room for doubt as to the exact physiological mechanisms involved there is no doubt that the glucose of the blood and tissues is locked up in an unavailable form and the cure is the immediate administration of glucose. Half an orange is sufficient for the mildest hypoglycæmic reaction, two or three pieces of candy or a tablespoonful of corn syrup suffice for the more severe, but when coma supervenes intravenous administration of 10 to 50 per cent sterile glucose solution should be undertaken.

The other danger is one which has been much neglected and consists in a progressive decrease in the carbohydrate tolerance of the patient. It occurs in those patients who are unnecessarily given insulin in order to eat an unnecessary amount of food in the form of the higher carbohydrates. Progress of the diabetes is to be feared in all insulin cases receiving more than 2,500 calories per day, not only because of the treatment the patient is instructed to take, but even more because of the loose, often careless, observance by the patient of the instructions he receives. Retribution in diabetes is slow, and probably this does not impress the physician with a few cases as forcibly as it does one who sees them in larger groups. Excessive consumption of food also has another aspect. When such large amounts of insulin as 100 to 200 units of insulin per day are used the cost runs from twenty to forty dollars per month, a sum which the patient is usually unable to pay and he therefore applies for free insulin. There can be no thought of restriction of free distribution of a remedy whose legitimate use saves the lives of many patients, converts them into economic assets to the country, and preserves their self respect, but the useless consumption of free insulin produces an insidious form of pauperization which it is unwise to encourage.

### SUMMARY

The various conditions which may arise in the diabetic requiring the administration of insulin are indicated, together with a discussion of the method of its use in these cases. The usefulness of insulin in non-diabetic cases is extremely limited. The dangers of insulin are discussed.

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PRIMARY CUTANEOUS GONORRHŒAL INFECTION.—V. Genner and P. Schultzer report the case of a medical practitioner who, while retracting a gonorrhœal prepuce, was slightly scratched by the patient's thumb; the hand was washed in soap and alcohol. Thirty hours later there was slight lymphangitis along the arm, followed by a small infiltration on the thumb, which on being incised two days later, gave vent to some serum. As the lymphangitis spread larger incisions were made, and some pus was found containing intracellular diplococci resembling gonococci. Later on severe articular pains set in affecting the shoulder; these were followed by involvement of the knees and considerable fever. Examination of the blood for the complement deviation test confirmed the existence of a gonococcal infection. As soon as the active joint symptoms ceased massage was used, and in spite of a long illness (from October to February) full use of the joints was recovered. There was never any suspicion that the disease was a septicæmia properly so called. The joint affections were typically blennorrhagic in character, being monarticular at the onset, spreading secondarily to other joints, muscles, and bursæ, and finishing as a resistant serofibrinous arthritis of the knees.—*Ann. de Derm. et de Syph.*, p. 856, August 1929.

# THE CLINICAL INTERPRETATION OF DIABETES*

BY JOHN R. WILLIAMS, M.D.,

*Rochester, N.Y.*

THE following is an abstract of a study of upwards of 500 diabetics with reference to a better means of control and interpretation. It is commonly believed that insulin causes the burning or utilization of 1.5 to 2 grams of glucose per unit. For the past six years the writer has co-operated with the Eli Lilly Company in the clinical testing of insulin. In this work one patient, whose metabolism is fairly constant and who is highly trained, has been used as a test case. The results obtained have been carefully checked and have invariably corresponded closely with the assays of the Lilly Company. The work which will be reported in a later communication indicates that one unit of insulin causes the utilization of approximately 4 grams of glucose, rather than 2 grams, as is commonly assumed.

The diet of normal individuals contains from 500 to 800 grams of glucose-forming food. One unit of insulin will burn approximately 4 grams of glucose. The normal pancreas makes from 75 to 200 or more units of insulin daily according to the food intake of the individual. When the pancreas fails to make sufficient insulin to care for the glucose content of the diet, diabetes results. That portion of the glucose which is not utilized and which exceeds the storage capacity of the body will be eliminated as urine sugar. The difference between the amount of glucose ingested and that excreted in the urine is the glucose utilization of the patient. The glucose utilization factor in a well treated case of diabetes is fairly constant and may be increased by the administration of insulin. In either a normal person or a diabetic the number of grams of glucose utilized, divided by four, will give the number of units of insulin made by the individual. This figure, hereafter designated as the insulin coefficient, is a fairly constant factor in the diabetic. Example: The diet contains 100 grams of glucose; 20 grams are eliminated in the urine; therefore 80 grams are utilized. The pancreas makes 20 units of insulin.

To determine the insulin coefficient of a patient, the number of units administered must be subtracted from the total number of units required for the utilization of the food. Thus in the above case if the patient were receiving 8 units daily his coefficient would be 20 minus 8, or 12 (written IC 12). The insulin coefficient is a fairly constant factor and changes slowly with improvement or decline. It is not materially affected by occasional indiscretions in diet, even in the presence of large amounts of urine sugar and high blood sugar levels, nor is it influenced by insulin administration.

A severe diabetic case is one in which the insulin coefficient ranges below 20; moderately severe cases range from 20 to 35; mild cases from 35 to 75. A diabetic may have a minus coefficient. Example.— The diet contains 100 grams of glucose, the urine 20 grams of sugar; 30 units of insulin are being administered daily. The insulin coefficient is -10. There are several explanations for this minus coefficient. (a) The insulin may be administered in too large a dose, in excess of the body requirements at a given time, and is eliminated in the urine, without serving any useful purpose; or (b) an infection or some other unsuspected disease may be present which destroys insulin; or (c) there may be an error in insulin administration; or (d) in diet. The insulin coefficient is a more valuable guide to the progress of an infection in diabetes than is the temperature curve or the leucocyte count. It has great prognostic value. It affords a most reliable check on the integrity of the patient who exceeds his diet or insulin dosage. It by far the best method of measuring the progress of a case and the efficiency of the treatment. A patient who can raise his coefficient from 5 to 10 units in a year is making satisfactory progress.

In making tests to determine the insulin coefficient, the patient should be thoroughly instructed as to its significance and the necessity

* Paper read at the annual meeting of the Ontario Medical Association in Hamilton, in May, 1929.

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for exact co-operation. The diet should be constant for at least three days if possible. The urine should be saved and measured with care. Urine sugars should be accurately determined. A slowly rising mid-morning blood sugar curve indicates that the patient is gradually exceeding his capacity to utilize glucose. The insulin coefficient is a far better method of differentiating spurious diabetes and renal diabetes from true diabetes than is the so-called glucose tolerance test. A glucose tolerance test is about as useful and reliable a method of determining the efficiency of the pancreas as is the hundred yard dash in eleven seconds a measure of the physical ability of an individual to walk five miles at a leisurely gait.

At the present time there is no clinical method in use which enables clinicians in one community to compare the efficiency of their methods with the clinicians of another community. Likewise there is no clinical method in use which enables physicians to accurately contrast or evaluate different therapeutic measures. The insulin coefficient method meets these requirements.

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## INFECTION OF THE UPPER RESPIRATORY TRACT AS AN ETIOLOGICAL FACTOR IN PULMONARY DISEASE*

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CLINICIANS who do not recognize infections of the upper respiratory tract as an etiological factor in producing disease in the lung are apt to be lead into serious error in their diagnosis of pulmonary affections. Many patients have been diagnosed as tuberculous, and have been sent to sanitariums, or advised to change their residence to a more agreeable climate, without any definite beneficial result. In many of these cases, on closer investigation, a focus of infection is discovered in the upper respiratory tract and excellent results follow its eradication.

A few of the leading works on medicine, such as Osler's Practice of Medicine, Tice's Practice of Medicine, and Nelson's Practice of Medicine make no reference to sinus infection as being a possible etiological factor in pulmonary disease. Rist pointed out the relationship between chronic cough and chronic disease of the nasal sinuses. Sargent reported that an incorrect diagnosis had been made in one-third of the cases of supposedly tuberculous soldiers in the French army, and that most of these mistakes were in men in whom more thorough investigation demonstrated chronic bronchitis associated with chronic infection of the nasal sinuses. Another factor which is responsible for the lack of interest in the subject is that it was formerly supposed that the paranasal sinuses were rudimentary at birth, and poorly developed in early childhood. The studies of Onodi, Shaeffer and Davis have proved that some of the cells are found well developed at birth. All of the sinuses may reach an advanced state of development very early in life, but some of them may never develop or may remain rudimentary throughout the entire life of the individual.

As the result of this lack of leadership on the part of medical writers the majority of the medical profession overlook the significance of paranasal sinus disease as a causative factor in pulmonary disease.

A few otolaryngologists, Sir StClair Thompson, Dean, Skillern, Hajeck and others have called attention to the rôle played by sinus disease in the causation of systemic disease. It has been demonstrated that cases of sinus disease very often go unrecognized for long periods of time, frequently for years, because of the lack of any outstanding symptoms; consequently they go unrecognized by the physician. It is only by careful search and inquiry into the history that one is able to trace the

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origin of a long unrecognized sinus infection. For instance, in the case of children who complain of frequent colds or protracted colds with expectoration, lassitude, who are undernourished, anæmic, who have nasal discharges, in whom tonsils and adenoids have been removed, you will find that many have some sinus involvement which has been present in latent form or with periodical attacks of nasal discharge dating back to an attack of scarlet fever, chickenpox, whooping cough, etc., but these sinus infections have in the majority of cases, been overlooked. There are, however, a number of clinicians who are working in large chest clinics, where ear, nose and throat departments are well established, who have had satisfactory results in their non-tuberculous chest cases because of their recognition of the fact that sinus infections are a causative factor in prolonging bronchial symptoms, and these men have stressed the importance of this subject.

We are all familiar with the experiments of Mullen and Ryder, which go to prove that there are two routes which connect the accessory sinuses with the lungs and bronchi. First, there is the lymphatic, or circulatory, route which can function even in cases of a sinus disease which does not discharge into the nose; and, secondly, the bronchial, or inhalation, route which is open to any substance reaching the nasal fossæ from the accessory sinuses or elsewhere.

As otolaryngologist to a large chest clinic, I have observed a large number of patients who come to the clinic suffering with symptoms which make them suspicious that they have something seriously wrong with their chests, possibly tuberculosis. Many of these patients had two or more of the following symptoms: cough; post-nasal discharge; loss of weight; general weakness; rise of temperature on exercise, or after a day's work; expectoration; dyspnœa; anæmia.

We have found that in the period between April 1, 1927, and April 30, 1929, there were 1,510 cases, of which 166 proved to be tuberculous, the remaining 1,344 being diagnosed as non-tuberculous. The major portion of these 1,344 non-tuberculous cases were diagnosed as bronchitis, subacute bronchitis, chronic bronchitis, bronchiectasis or asthma, and the re-remainder showed no evidence in the chest sufficient to make any clinical diagnosis possible.

The following is a brief summary of these cases as arranged in groups:—

| | *Chest Findings* (Clinical) | *X-Ray Findings* (Chest) | *Upper Respiratory Findings* (Sinuses, Nose and Throat) |
|---|---|---|---|
| Group 1. ..... | Absent | Absent | Present |
| Group 2. ..... | Present | Absent | Present |
| Group 3. ..... | Absent | Present | Present |
| Group 4. ..... | Present | Present | Present |
| Group 5. ..... | Present | Present | Absent |
| Group 6. ..... | Absent | Present | Absent |
| Group 7. ..... | Present | Absent | Absent |

In my series I have numerous examples of each of these groupings, but time does not permit me to quote them. I shall, however, report on this subject with complete details in the near future.

Under the heading of Chest Findings, the following were present: (1)impairment of resonance; (2) hyper-resonance; (3) increased vocal resonance; (4) slight impairment of vocal resonance in both apices; (5) infrequent crepitant râles which did not disappear following cough, elicited over the apices; (6) bronchial breathing; (7) fine râles and coarse râles at bases; (8) sibilant râles all over the chest; (9) bronchial râles.

In a large number of cases we found the pathological manifestation more commonly in the base of the right lung. This is easily explained by the direct drainage of the infectious secretions of the nose and throat through the larynx, trachea, and right bronchus to the right lung.

Where there was nasal obstruction the patient could not breathe properly and deeply, and the apices of the lungs were involved owing to deficient expansion of the upper lobes.

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The radiographic findings vary a great deal, but the following are a few that were sometimes present. They can be divided conveniently in three groups:—

1. (a) The nodes at the hilus enlarged and showing various shades of density. No deposits of calcareous substances observed about the nodes in the parenchyma.

   (b) The area of the hilus shows a characteristic shadow through which the nodes are observed. This indefinite shadow extends into the surrounding parenchyma and seems to blend gradually with the normal lung tissue.

   (c) A haziness and thickening of the bronchial shadow from the base to the hilus appears as the most frequent x-ray finding.

   (d) Shadows varying in degree from slight haziness to consolidation.

The above findings are more commonly on the right side, particularly in the base of the lung, but have also occurred on the left side.

2. (a) Another type of case is that in which this process involves the upper lobes, and the density is shown along the mediastinum on both sides. These shadows extend outwards and not infrequently have a density that resembles a slight degree of consolidation.

   (b) The bronchioles and lymphatics are dense and fuzzy in outline.

When this condition exists, moist and sibilant râles may be heard, and increased tactile fremitus and whispered voice sounds are noted. This picture is one of infiltration of the upper lobes, similar to that found in tuberculosis, except for the absence of the mottling and beading common in that disease. It clears up rapidly after the nose and throat symptoms have disappeared.

3. Occasionally, a composite picture of the two types of x-ray findings is seen. Here, both the apices in the upper lobes and the bases are involved with the diffuse bronchial thickening, with a density in the parenchyma, which represents more or less infiltration. Occasionally, there are small areas of density on the background of lesser density that are evidently small abscesses or dilated bronchioles.

A patient presenting this picture is usually to be considered as suffering from diffuse bronchitis with areas of bronchiectasis. This latter condition does not resolve so quickly, and the small abscesses or dilated bronchioles cast shadows for months after the nose and throat conditions have cleared up.

The outstanding features of these chest conditions, secondary to the nose and throat conditions, are the apparent chronicity, the lack of calcareous deposits in the lung tissue, hilus nodes, the rapidity with which they clear up under proper treatment, and the little residue left after resolution has occurred. A chest condition that resembles tuberculosis clinically and radiographically, of recent origin, following influenza, etc., will show, after a few weeks of treatment, no pathological lesion whatever.

Nasal sepsis can affect the lungs or lower respiratory tract in three ways: (1) By direct extension of the inflammation to the larynx, the trachea and bronchi, or by infection through the blood or lymphatic streams; (2) by aggravating or increasing an existing lesion of the lungs; (3) it may be part of a general infection, in which both the upper and lower respiratory tracts are involved. These items are self-explanatory, and as they are all familiar to you it is not necessary for me to enlarge upon them.

One must not forget that sinusitis and bronchitis frequently originate at the same time, and that the persistence of the sinus condition prevents the bronchial condition from getting better. You will find that the majority of cases of bronchiectasis originate in early life. The following is a short summary of the most common upper respiratory infections, divided into groups, found in my series of 1,344 non-tuberculous cases:—

(a) A group of 464 cases with deviated septa, spurs on septa, and hypertrophied turbinates. Of this group 51 had total nasal obstruction, more or less all the time. The remainder, 413, had partial blockage, with occasional total blockage. This group had attacks of frequent "colds" in the head, but no suppuration.

(b) 582 cases. Of these 50, mostly children,

showed nasal discharges; 105 had one or more sinuses involved; the most commonly affected sinus was the antrum. These sinuses showed no discharges. Of this latter group, 13 had polypi in the nasal chambers; the remaining 427 showed post nasal discharges of varying character in adults. In the greater number of this group one or more sinuses were involved. A small percentage of this group had post-nasal discharge for which no definite origin could be established.

(c) 76 cases, presenting various types of ulceration of the nasal mucous membrane.

(d) The remainder had the following conditions; diseased tonsils, enlarged tonsils and adenoids, elongated uvula, increase of hypertrophied tissue of the pharynx, pyorrhœa, caries, granular pharynx, and various conditions of the larynx.

Sinus infection and acute bronchitis may be produced by the same cause, such as influenza, pneumonia, diphtheria, scarlet fever and measles, which may attack the entire respiratory tract, upper and lower, at the same time. If resolution does not occur in the sinuses, a chronic condition is established, and the pus, by its continually dropping into the air passages, will account for the acute bronchial condition becoming a chronic one and in time giving rise to bronchiectasis. The natural tendency is for ordinary bronchitis to undergo resolution, unless it is kept active by discharge of a chronic sinus infection. Acute bronchitis and broncho-pneumonia, though to a less degree, are usually phases of infections which involve the whole of the upper respiratory membrane, often including the sinuses.

I shall not go into the question of treatment of the sinus infection, as this is well known to you, but experience shows that enough cases are relieved, improved, or cured, to encourage one to continue his efforts towards complete eradication of sinus infection. Even if a cure is not always obtained, eradication of the focus lessens absorption, and promotes proper drainage. In early cases of chest disease the thorough removal of all foci of infection results in cure. This is particularly so in the bronchitis following infectious fevers.

It must have occurred to many of you that there may be some other cause which is a contributing etiological factor in sinus disease. The conclusions of Daniels, Armstrong and Hutton, who fed rats on a diet deficient in fat soluble vitamin A, were that all these animals were very prone to infection. All of them had purulent inflammatory changes in the sinuses, middle ear, or eye. This lack of vitamin A may possibly be a factor contributing to the poor resistance to some infections, but this idea is at present theoretical.

## CONCLUSIONS

1. The laryngologist should not hesitate to call the aid of the physician, and the physician should more frequently consult the laryngologist, both for diagnosis and treatment in non-tuberculous lung lesions. This broader view of the case is taken with beneficial results to the patient, preventing chronic bronchial diseases from being treated over long periods with cough mixtures and sedatives without results.

2. It is the duty of the laryngologist and the physician to recognize this close interrelationship between these two systems, to take every opportunity they can of reporting cases before medical societies, so that the profession will gradually realize the importance of upper respiratory infection as a very important causative factor in pulmonary disease.

3. It is important to secure a very thorough history in broncho-pulmonary disease. In doing so you will find that it very often proves to be a sequel of some infectious fever, which may also be the cause of the sinus infection.

4. The persistence of the sinus infection which has remained unrecognized is the fertile cause of the chronicity of the bronchial infection.

5. Nasal discharges in children in whom tonsils and adenoids have been thoroughly removed probably arise from the sinuses, and should not be overlooked.

6. No condition of the chest should be finally diagnosed without a thorough search for foci of infection in the head.

7. Many cases have been diagnosed and treated for pulmonary tuberculosis and bronchiectasis because the internist paid no attention to the upper respiratory tract. Therefore, in all doubtful cases, in the absence of the bacillus of tuberculosis, the case should be submitted to an otolaryngologist for further investigation and treatment.

8. It is quite common to see young adults and children with frequent attacks of protracted coughing, in the absence of chest lesions. The examination of nose and throat will reveal a chronic catarrhal condition of the mucous membrane of the nose, pharynx, or larynx, without any sinus condition.

9. The eradication of a focus of infection, as a suppurating sinus, or the removal of a mechanical obstruction in the nose, will permit a poorly developed or a pre-tuberculous subject to fight broncho-pulmonary infections much better.

10. One must not accept the patient's history of negative nasal trouble alone without investigation of the sinuses.

11. The earlier you recognize the foci of infection, that is before organized pathological changes take place in the lung, the quicker the patient will return to normal health.

12. No diagnosis should ever be finally made on the evidence of x-ray plates of the chest and sinuses.


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## ACCESSORY SINUS DISEASE IN CHILDREN


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DURING the past two years the author has had an opportunity of studying a large number of children suffering with nasal trouble at the Hajek Clinic at Vienna, and while associated with Dr. Lempert in his private practice in New York City.

All of these children came with practically the same complaints, constant "head colds" with profuse nasal discharge, mouth breathing, frequent running ears, and periodical attacks of sore throat. Careful history and examination brought out some characteristic and important facts. The ages ran between two months and fourteen years. The children had been suffering with head colds, mouth breathing, and nasal discharge ever since the mother could remember; many of them had already been operated on by removal of tonsils and adenoids; some had been operated on several times. In a large number of the cases the little patients were unrelieved by the operations; in some, indeed, they had aggravated the condition, the discharge and mouth breathing being worse than before. One or more attacks of otitis media were very common, and in some the ears were continually discharging. Malnutrition, rickets, sleeplessness at night, and enuresis were frequently associated factors. In a large number of the cases the tonsils and adenoids had already been removed; when present they were hypertrophied and diseased. A postnasal drip of thick yellow or greenish yellow tenacious pus was invariably present. The ears in all the cases showed chronic catarrhal changes—retraction, clouding, and often chalky deposits. The mobility, as tested with Bruening's "Ohrlupe," was in the majority of the cases only slightly decreased, and the hearing was quite good, even in one case where the drum and ossicles were completely destroyed. Examination of the nose showed a condition which was present in practically all the cases. The inferior turbinates were swollen and congested and bathed in thick muco-pus. When the turbinates were shrunk by the application of adrenaline (1-1000) or ephedrine (3 per cent),

the muco-pus was found in the inferior meatus and flowing backward into the nasopharynx. When removed by suction it came away almost like a cast of the inferior meatus. Every part of the nose was investigated with a long straight suction cannula to complete the examination. Following the removal of the secretion the children were able to breathe through the nose as never before.

X-ray examination in all cases showed clouding of both antra; some cases showed evidence of polypoid change and thickening of the mucous membrane. No cases of involvement of the frontal or sphenoid sinuses were found and very few instances of ethmoiditis. At no time did the x-ray examination show evidence of empyema of the antra. Antroscopic examination with the Spielberg antroscope showed thickening and congestion of the mucous membrane, and occasionally small and large polypi. Large polypi are often found in antroscoping the adult antrum.

Two forms of treatment were employed: (a) palliative; and (b) surgical. Palliative treatment was tried in every case and given a fair trial, to be followed by surgical measures in case the conservative treatment failed. Treatment consisted of daily suction and exposures to radiant heat. The mother was instructed to instill 10 drops of a 25 per cent solution of argyrol into both nostrils twice daily, and was taught how to instruct the child in the proper use of the handkerchief. The proper training in blowing the nose is very important, and as most children do not know how to, or never, blow the nose, this results in an accumulation and stagnation of pus in the nose. Following the suction the nose was sprayed with a 10 per cent argyrol or neo-silvol solution. Radiant heat was supplied by means of the infra-red lamp. The time exposure and distance depended on the individual tolerance. When no improvement followed two to three weeks of conservative treatment surgical measures were resorted to. In all infants and in the majority of young children it was not necessary to resort to these. Suction treatments and radiant heat were sufficient to effect a cure in nearly all cases.

Surgical treatment consisted in puncturing one or both antra and irrigation with normal saline. Occasionally, very good results were obtained by irrigating with 2 per cent mercurochrome, after washing with normal saline. The success of this form of treatment depends invariably upon the size of the opening in the naso-antral wall, and upon the length of time it remains open. In no case did the treatment fail where the opening was large and remained patent for six weeks or more. It is the aeration and drainage afforded by the opening that cures the sinusitis. The number of irrigations depended on the individual case. In many, the removal of the secretion by suction and the inflation of air into the sinuses was more effective than the wet treatments. During an acute exacerbation of the sinusitis all local treatments, other than the instillation of ephedrine (1 per cent) in albolene into the nose several times daily, was strictly avoided.

The question of anæsthesia is very important. In the younger children general ether was used by the open air or intra-tracheal methods. The latter was found ideal, because it avoided the placing of a postnasal plug to prevent aspiration of blood. It is important that the laryngeal tube fits snugly but without pressure. This can be supplemented by placing gauze loosely around the tube in the mouth. In older children local anæsthesia was preferred. The inferior meatus was packed with a long strip of cotton saturated in equal parts of 10 per cent cocaine and 1-1000 adrenaline. This was allowed to remain 15 minutes. When the anæsthesia was not complete, it was supplemented by the application of a small amount of cocaine mud. The naso-antral wall was broken down with a West nasal chisel. The antrum was entered by a slight blow on the chisel, which was then rotated upwards and downwards producing a large window. This was enlarged in all directions with biting forceps. The rough edges were smoothed off with a rasp or with a Halle burr; all debris was removed and the antrum thoroughly inspected with the antroscope. No packing was introduced and the patient returned to bed. Post-operative bleeding was quite rare. When it did occur it was quite easily controlled with nasal tamponade. Two cases required a tight post-nasal plug for twenty-four hours in addition to the nasal packing. The bleeding in the above cases occurred eight and ten days after the operation respectively. No irrigations were

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done until all local reaction had subsided. The secretion was removed by suction; fresh hot packs of argyrol (10 per cent) were inserted and exposure to radiant heat was given for 15 to 20 minutes. Neo-silvol (20 per cent) was prescribed for home treatment.

A statistical account merely lengthens the paper and it is doubtful if any real practical information is derived therefrom. I shall, therefore, only cite a few selected cases, to illustrate the various problems and the methods used in dealing with them.

CASE 1

S. R., male, 12 years of age. The mother said that the child had had nasal colds since infancy. Both ears showed a foul discharge, which dated back to infancy. Tonsils and adenoids were removed one year ago. Ever since the operation there were nasal colds, and profuse nasal discharge, considerably worse than before the operation. The child was restless, undernourished, slept poorly, and wet the bed. Examination of the nose showed the inferior turbinates to be congested and pressing against the septum, completely blocking the inferior meatus. The turbinates were bathed in thick muco-pus. The tonsils and adenoids had been well removed. The ears showed posteriorly marginal perforations, with yellow thick pus extremely foul in odour. The hearing was but slightly affected. There was no spontaneous nystagmus or post pointing. The Romberg test was negative. The caloric test showed normal labyrinths. X-ray examination showed clouding of both antra. The remaining sinuses were well illuminated. The boy was treated conservatively for two weeks without any apparent improvement. Under local anæsthesia both antra were punctured and examined with the antroscope. The mucosa was markedly polypoid and bathed in thick yellow pus. The pus was aspirated and a little 20 per cent neo-silvol sprayed in. After the reaction had subsided treatment was carried on at the office. Secretion was removed from the nose and argyrol and radiant heat applied. The ears were treated by removing the secretion with an attic cannula wash with peroxide, followed by ether. After two months' treatment the patient had no nasal discharge, breathed well through his nose, and only a slight moisture was present in the ears, the foul odour having disappeared.

In this case various antiseptics were used for a time for irrigating, such as mercurochrome (2 per cent), acriflavine (1-1000), St. 37, without any apparent superiority over the dry treatments. X-ray examination after two months' treatment showed the same cloudy antra, but antroscopy showed the almost complete disappearance of polypi. The lining membrane, however, was still thick and congested in parts.

It is evident from the history that the preliminary tonsil and adenoid operation had aggravated rather than improved the condition. This is explained by the fact that the removal did not provide improved drainage for the sinuses. Rather, the raw operated surfaces become infected by the discharge and this was the cause of the aggravation of symptoms. In every case of sinus disease in children better results will be obtained if the attention is directed toward the sinus condition first, and only when there is considerable improvement should the tonsils and adenoids be removed.

CASE 2

M. B., male, 3 years old, who had suffered from constant head colds and profuse nasal discharge. The tonsils and adenoids had been removed three months previously. The mother said that the discharge and head colds were worsse than before the operation. For the past week the child had had a running ear. Examination showed swollen inferior turbinates covered with thick pus. The right ear was normal; the left ear showed otitis media purulenta acuta, with spontaneous perforation in the upper posterior quadrant. The tonsils were well removed. The pharynx was covered with tenacious muco-pus. Examination of the postnasal space showed no adenoid tissue.

The patient was treated conservatively for three weeks. When last seen there was no nasal discharge; the child breathed through the nose and both ears were dry.

CASE 3

M. G., female, aged 22 months, who had constant nasal colds, nasal discharge, with mouth breathing. There had been discharge from the right ear for one month. The child was very restless at night; temperature, 102.6.° Examination: left ear, O.M.P.A., with bulging in the posterior superior quadrant. The right ear showed a large central perforation, with profuse thick pus. Tenderness was lacking over both mastoids. The left drum was incised and the rhinosinusitis treated conservatively for two weeks without any apparent improvement. Puncture and irrigation was advised, but refused by the parents. Conservative treatment was carried on for the next three months. Quartz-light exposures were given and "viosterol" added to the diet. The child was treated thrice weekly, with slow but progressive improvement. The ears had cleared up. There was still a small amount of nasal discharge, but the colds were less frequent and the child breathed through the nose. At this time the removal of the tonsils and adenoids was considered appropriate. When last seen, two months after the operation, there was no nasal difficulty whatsoever.

This case demonstrates that where the tonsils and adenoids are present and attention is directed toward the sinusitis primarily the condition is not aggravated, but on the contrary this treatment helps to cure the sinus condition. Undoubtedly, quicker results could have been obtained had the parents allowed puncture of the antra. It shows however what can be obtained with persistent conservative treatment.

CASE 4

A male, aged 8, who was seen in consultation with Dr. David Esser. His complaints were epistaxis, frequent head colds, profuse nasal discharge, and crusting inflammation around the nose. The tonsils and adenoids had been removed one year before, and according to the mother the symptoms were unrelieved.

Examination revealed a chronic eczema of both nasal vestibula. The upper lip, nose, and skin over both cheeks were swollen, bluish and puffy. There was no elevation of temperature. The inferior turbinates were boggy and bathed in yellowish muco-pus. When the membranes were shrunk with ephedrine (3 per cent) and the secretion removed, he was able to breathe much better. Anterior rhinoscopy revealed the presence of a large ragged mass of adenoid tissue. The tonsils had been well removed. Transillumination was negative. Conservative treatment had been carried on quite diligently by the attending physician without any improvement. Antrum puncture and irrigation was negative. It was decided to remove the adenoid tissue. Within one week following the removal, there was no nasal discharge, the boy breathed through the nose, the swelling of the nose and cheeks disappeared, and the eczema was healed.

Tonsillectomy is usually well performed, *i.e.*, the tonsils are completely removed. One should strive to do the same in adenoidectomy, particularly in young children where a small amount of adenoid tissue makes a considerable difference.

CONCLUSIONS

Accessory sinus disease in children is frequently associated with the presence of diseased tonsils and adenoids, although it may exist independently. Each case should be studied individually. In a large number of cases the sinusitis is unrelieved, even aggravated, by the preliminary removal of tonsils and adenoids. A so-called "running cold" should not be regarded as a rhinitis or coryza, but as a rhino-sinusitis. Eighty per cent can be cured by conservative measures only. Radical operations are unnecessary. Children, also many adults, should be taught how to blow the nose properly. Chronic sinusitis in adults can be traced to infection in childhood that has been left untreated. More emphasis should be placed on complete adenoidectomy.

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# ATYPICAL MASTOIDITIS*

## WITH REPORT OF CASES

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DURING the influenza epidemic in the winter and spring of 1928-29 many ear complications of unusual character and severity were seen, both in hospital and private practice.

It is my purpose to review briefly some of the atypical forms of mastoiditis observed at that time. These atypical cases always cause great difficulty in making a correct diagnosis, and are often overlooked until some more or less serious complication occurs.

Briefly the signs and symptoms of what is usually considered typical mastoiditis without complications are as follows: a history of acute rhinitis, followed shortly by earache; conductive deafness; perforation of the drum head; and purulent discharge. The pain, which is in and about the ear, is not relieved by this discharge and is often worse during the night. The temperature ranges between 99° and 101°; rarely is it over 102.° Tenderness and swelling over the mastoid periosteum may be noted, but the most characteristic site of swelling is over the posterior superior wall of the external auditory canal. The x-ray picture shows an increased density with blurring of the cell walls, and there is a leucocytosis of moderate degree.

In a considerable number of cases of mastoiditis, however, many of the above signs and symptoms are entirely absent, and through an error in diagnosis the true condition may be overlooked until some serious or dangerous complication arises. One is often surprised at operation to find such extensive disease with comparatively mild symptoms. I will briefly cite five cases illustrating different atypical conditions.

CASE 1

B. B., female, aet. 6, ill two days with influenza, and severe pain in left ear. The drum was red but not bulging. Paracentesis produced no discharge from the ear and no relief from pain. The temperature was 100° to

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102.° The child remained very ill. Two days later the drum was again incised, but there was no discharge; pain and mastoid tenderness were increased. By the fifth day a boggy swelling developed over the mastoid, and at operation a sub-periosteal abscess was found, with a fistula into the mastoid process which was entirely broken down. In this case there never was any discharge from the middle ear at any time, although the drum was incised twice. This type might be spoken of as acute fulminating mastoiditis.

### CASE 2

A male, aet. 17. Four days after influenza, pain and partial deafness developed in the right ear. There was no discharge. The symptoms quickly subsided, but noises and deafness persisted. Three weeks later the boy was attacked by acute pain and tenderness over the same mastoid, and in 48 hours a fluctuating swelling developed. At operation, a sub-periosteal abscess was found, with a fistula leading into an extensively diseased mastoid. The drum was not incised, and at no time was there any perforation of the drum or discharge from the ear.

### CASE 3

A male, aet. 22. One week after influenza, he developed some discomfort and deafness in the left ear. The ear began to discharge 24 hours later. This continued for 18 days, when the perforation healed, but the hearing did not return and the patient felt ill and languid. Ten days after the ear dried up a tender fluctuating swelling developed over the mastoid, which at operation proved to be a sub-periosteal abscess connected with a broken down mastoid.

This patient complained of malaise and deafness all the time, but there was never any definite pain, and he attended lectures at the university up to the day of operation.

### CASE 4

E. H., male, aet. 17, developed acute suppuration of the right ear, which continued with lessening discharge and normal temperature for 20 days, when he was suddenly seized with severe pain radiating over the whole side of the head, but more marked in the temporal region. The temperature rose to 101.° There was no superficial or deep tenderness over the mastoid proper, but far back over the emissary vein a small tender spot was found. At operation the mastoid cortex was found to be very hard and thick. The underlying cells were infected, and a large perisinus abscess was found extending above the knee of the sinus.

This case is atypical because at no time was there any tenderness over the mastoid process. This is undoubtedly due to the fact that the cortex was unduly hard and it was very difficult for the infection to reach the surface.

### CASE 5

B. C., aet. 6, had influenza followed by suppuration of both ears which gradually dried up. In four weeks both ears were dry, but the child remained peevish and rather deaf. Two weeks after the left ear dried up a tender painful swelling developed in front of and above the ear, extending over the parotid and temporal region. At first a parotid abscess was suspected, but with a history of previous ear discharge and some sagging of the anterior superior canal wall an attempt was made to drain the pus through a high mastoid incision. A sub-periosteal abscess was found, with a fistula extending into the cells in the zygoma which were entirely broken down. The remaining mastoid cells were not infected.

This case is atypical because at the time of operation there was no discharge from the ear, and no swelling or tenderness over the mastoid proper, the maximum point of tenderness being anterior to and above the tragus.

### SUMMARY

1. Extensive mastoid disease may occur without any obvious middle ear suppuration.

2. Pain, the most reliable of mastoid symptoms, may be absent.

3. There may be complete absence of tenderness, swelling or fever, even in the presence of extensive necrosis.

4. Every patient complained of deafness.

5. We must always be on the alert for cases of atypical mastoiditis if we are to avoid its dangerous complications.

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THE MARVELS OF FISH LIFE.—The news that Dr. William Beebe has been appointed the new director of the Tropical Research Station on Nonsuch Island, Bermuda, will interest all nature lovers, since no man has done more in recent years to help the general public—the untravelled mass of humanity—to appreciate something of the marvels of the under-water world. Dr. Beebe is a scientist who dons the diving helmet, descends to the depths, and regains the surface, bringing with him true stories and pictures of the fairyland of fact. The objects of the Bermuda Research Station are not to make a mere compilation of lists of species dredged, but to study the life histories and habits of the fish. Many interestaing matters have already come to light. One is the peculiar uniformity of fish life throughout the world in waters of a standard depth—half a mile or so below the surface. In this chilly region of cold and stygian darkness the same fish occur off Bermuda as off Japan. An example of the aforementioned uniformity in the distribution of fishes at a specified depth is the rediscovery by Dr. Beebe of that most remarkable of all fish, the parasitic angler, a creature first captured a few years ago off the coast of Iceland, and which presents one of the strangest instances of natural grafting that has yet been brought to light. The female of the species is a heavily built fish about a yard in length, whilst the male measures little more than three inches. The minute husband attaches himself by means of his suctorial mouth to the under surface of his bulky bride, to whom he eventually becomes grafted and whose blood supply he therefore shares. The male, at first a self-supporting fish with a fair complement of digestive organs, slowly degenerates into a mere bag containing the reproductive glands which crowd out the stomach, intestines, and swim-bladder. Mr. Tate Regan, the Director of the Natural History Museum, has had prepared a beautiful series of models, showing not only the external appearance of this strange union, but also the "inner workings."

# LA DIPHTERIE CLANDESTINE DANS NOS CRECHES[1]

## SES LOCALISATIONS NASALES ET AURICULAIRES: SES RELATIONS AVEC LE TAUX DE MORTALITÉ INFANTILE.

PAR DANIEL LONGPRÉ,

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*à Liesse, (près Montréal)*

COMME charnier à bébés, il y a d'abord, paraît-il, Calcutta puis, pas très loin Montréal. La province de Québec toute entière voit périr ses petits par milliers. Donner comme cause première de ce massacre des innocents une natalité presque phénoménale est éviter la question. Les gens du Québec font beaucoup d'enfants mais ils les font sains. Le *nombre* de morts est nécessairement plus grand là où il y a plus de naissances; nous ne voyons nullement pourquoi la *proportion* de survivants serait moindre qu'ailleurs.

Nos Crèches certes participent à cette mortalité élevée. Avouons qu'elles en sont un des éléments. On se plaît à dire que nous héritons du produit de conceptions clandestines, que nos hospitalisés ont subi les affres de grossesses maudites où tout a été d'abord mis en œuvre pour empêcher l'arrivée à terme puis où devant l'insuccès du crime d'avortement le ventre a été comprimé pour cacher la faute. Enfin nombre de nos petits voient le jour dans des circonstances défavorables, et nous sont apportés après parfois des jours sans soins quand ils ne sont pas déposés sur quelque perron, ou abandonnés à la petite gare de Liesse.

Mais nos enfants arrivent sains, du moins dans l'immense majorité des cas. C'est dans les jours ou les semaines qui suivent que la morbidité apparaît. Grande chez nous, elle l'était aussi il y a peu d'années dans la plupart des institutions du genre de la nôtre.

Le problème des Crèches a fait l'objet de nombreuses études. Nous voulons apporter notre modeste contribution. Nous ne nous flattons nullement d'avoir trouvé la clef du problème. Bien au contraire, notre travail tendrait à démontrer que le problème est multiple. A savoir: que le "mal des crèches" est un état symptomatique et secondaire qui peut être entraîné par nombre de causes. Les recherches que nous avons fait semblent indiquer que la diphtérie clandestine, nasale, pharyngée ou auriculaire en est une, en est une importante et en est une dont l'on ne connait pas suffisamment l'importance comme facteur de morbidité et de mortalité.

En Allemagne les troubles généraux que nous rencontrons chez nous et que nous avons analysés, ont été étudiés par Czerny sous le nom de "Maladie Lactée" et par Finkelstein sous celui de "Rupture des Equilibres".*

Une autre explication, la plus accréditée généralement, veut que les enfants meurent tout simplement de gastro-entérite infectieuse, l'énorme majorité de ces enfants présentant durant leur ultime maladie des symptômes digestifs plus ou moins accentués: vomissements et diarrhée. Citons encore une théorie plus récente appliquée à certains de ces cas: la fièvre du lait sec. Et combien d'autres encore.

Devant tant de routes nous ne savions que choisir. Aussi décidames-nous, en entrant à la Crèche d'Youville, d'en agir à la façon de Descartes, de faire table rase de tout ce qui avait été dit jusque-là sur "le Mal des Crèches," bref de commencer par allumer nous-mêmes notre lanterne.

La Crèche d'Youville hospitalise régulièrement plus de sept cents enfants, de la naissance à six ans, dont plus de quatre cents nourrissons de la naissance à vingt mois.

On y enrégistrait comme dans nombre de crèches européennes ou américaines une mortalité excessivement élevée. Or l'étude des

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***Nous traduisons les mots "Milk Injury" et "Disturbance of Equilibrium" du texte anglais de J. Thompson, The Clinical Study of Sick Children, p. 194.**

statistiques des trente dernières années nous montra que la mort survenait, dans l'énorme majorité des cas, dans les six premiers mois. L'examen clinique des nourrissons ainsi affectés nous permit d'établir une symptomatologie pratiquement identique pour tous et une histoire se résumant à ceci:

*Né* de parents inconnus.

*Entré* à la Crèche à l'âge de quelques jours.

*Santé* apparamment bonne (pour la majorité, du moins).

*Sommeil;* bon. *Appetit;* bon.

*Vomissements;* aucuns. *Selles;* normales.

Doux ou trois jours après l'admission, légère poussée de température, refus de boire, agitation, pleurs semblant causés par la douleur, vomissements accompagnés de selles panachées.

A l'examen, rien à noter, si ce n'est une *légère angine rouge* accompagnée presque inévitablement d'un coryza séreux devenant quelquefois franchement purulent. Les symptômes principaux et qui sautent aux yeux sont, refus de boire, vomissements, et diarrhée.

Evolution: persistance des même troubles entraînant l'amaigrissement, le tirement des traits; quelques jours après, mort soudaine, sans prémonitoires particulièrs. Parfois la maladie passe à la chronicité ou à la sub-acuté; l'enfant s'en va vers l'athrepsie. Après quelques mois, s'il n'a pas succombé, il se met subitement à prendre le dessus.

Les apparences plaideraient donc en faveur d'un trouble intestinal plus ou moins grave, d'origine probablement infectieuse. Quelle en était la cause?

D'autre part nous savions à ce moment que, prenant nettement parti dans une vieille querelle, Maurice Renaud dès 1921 avait attiré l'attention des pédiâtres sur la fréquence et l'importance des otites moyennes suppurées insidieuses chez le nourrisson. Il prétendait, après des recherches bien conduites, que "les états infectieux, dont elles sont une complication très grave, jouaient un rôle considérable dans la pathologie du premier âge."[1] Deuxièmement, nous savions que divers anatomo-pathologistes n'avaient pu déceler la moindre lésion anatomo-pathologique dans le tube gastro-intestinal de presque tous les nourrissons morts avec l'étiquette "gastro-entérite." Enfin nous savions (mais cela n'était qu'hypothèse, que quelques travaux allaient bientôt appuyer), que selon McKim Marriott, de Saint Louis, Missouri,[2] il était d'expérience clinique que un grand nombre de troubles attribués jusque là au système digestif, étaient dues à des lésions infectieuses situées, quelquefois très loin de l'intestin, et, la plupart du temps, dans l'oreille moyenne et la mastoide.

La salle d'autopsie est en définitive le plus instructif des amphithéatres. Aussi est-ce là que nous allâmes chercher la confirmation ou l'infirmation des avancés énoncés plus haut. Disons dès maintenant que les recherches faites par nous nous ont conduit aux mêmes conclusions que Maurice Renaud. Dans les soixante autopsies pratiquées sur des enfants morts avec les symptômes décrits tout-à-l'heure, soit apparemment de gastro-entérite, nous n'avons trouvé de lésions intestinales que deux fois: une fois une lésion congénitale du gros intestin; une fois un abcès appendiculaire chez un enfant de trois semaines. Le tableau s'établissait ainsi:

| | |
|---|---|
| Pyelo-néphrite | 1 |
| Abcès perihépatique | 1 |
| Broncho-pneumonie | 7 |
| Tuberculose pulmonaire | 1 |
| Otite et mastoidite | 50, |

soit dans 83 per cent des cas.

Or, chose remarquable, dans 68 pour cent de ces cas, nous relevions les lésions concomitantes suivantes: péricardite, foyer hémorragique pulmonaire, et congestion des capsules surrénales.

Ces constatations concouraient donc avec celles de Maurice Renaud. Sans éliminer complètement la gastro-entérite franche, elles nous semblaient plaider plutôt en faveur d'une toxi-septicémie apparemment d'origine le plus souvent otitique, et ayant entrainé des symptômes digestifs secondaires.

Nous venons de dire que ces constatations n'éliminent pas complètement l'infection intestinale franche et autonome. Cette série d'autopsies ne nous en montrant point d'exemple, nous ne saurions en conclure qu'elle n'existe pas. Mais il nous semble à tout le moins permis d'en induire que le champ de la gastro-entérite véritable, cause, et non effet, doit être singulièrement rétréci, au bénéfice d'entités pathologiques jusqu'ici négligées. Comme question de fait, il s'en rencontre certes à la Crèche d'Youville, comme partout ailleurs. Mais il nous semble désormais facile de diagnostiquer différentiellement la maladie intestinale d'avec le symptôme intestinal secondaire.

1o. Cliniquement, nous ne rencontrons la maladie intestinale, la gastro-entérite apparemment essentielle, que strictement chez les grands enfants. Si nous osions risquer une hypothèse nous dirions que ce la tient possiblement au fait que étant donné l'âge et la robustesse de ces enfants, la pasteurisation du lait qui leur est donné est moins surveillée et moins parfaite.

2o. Au contraire de la gastro-entérite purement symptômatique et secondaire, la gastro-entérite maladie répond bien à un traitement dirigé sur le tractus digestif.

En septembre, 1926, nous en avions une courte épidémie: 32 cas, sur quoi 2 morts seulement. En juin, 1927, 7 cas, pas de décès. En septembre, 1927, 16 cas, une mort; soit une mortalité totale de moins de 6 pour cent, à comparer avec les 65 pour cent de la "variété symptomatique".

La grande erreur de tous les temps semble donc, à notre avis, de confondre les deux variétés de diarrhée ou si l'on veut de gastro-entérite et de prendre pour une gastro-entérite essentielle ce qui n'était que symptômes digestifs. Il nous apparaît possible au pédiâtre expérimenté de faire désormais le départ et le diagnostic différentiel entre deux états différant non seulement par les symptômes mais encore par les constatations anatomiques, le traitement, et la terminaison probable.

Mais notre but en ce travail n'est pas l'étude comparée des deux entités, mais bien de raconter à quoi nous ont conduit les recherches faites *post* et *ante mortem*.

En mars, 1927, nous étions tombés sur un article de James B. Costen,[3] où l'auteur relatait les observations cliniques de deux cas de mastoidite survenus chez deux enfants présentant des symptômes superposables entièrement à ceux que prèsentaient occasionnellement les pensionnaires de notre Crèche. Les lésions mastoidiennes décrites consistaient en la présence d'une grande cavité tapissée d'une espèce de fausse membrane. Ensemencée, cette fausse membrane avait donné des bacilles diphtériques virulents. Ces lésions décrites par M. Costen correspondaient en tous points à celles que l'un de nous avait remarquées tant de fois au cours des nombreuses antrotomies pratiquées depuis juin 1926. Le pus mastoidien et le pus otique de nombreux petits malades, prélevé soit lors d'une intervention mastoidienne soit par ponction aspiratrice de l'oreille moyenne, fut ensemencé. Nous fimes encore des cultures de sécrétions du nez et de la gorge de certains de ces malades. Disons tout de suite que ces malades ne furent pas triés. Pendant quelques semaines nous fimes des prises chez de petits malades dont les symptômes généraux allaient du simple amaigrissement jusqu'à l'athrepsie avec selles vertes diarrhéiques. Plusieurs ne présentaient que d'occasionnelles poussées de température. Certains n'offraient que des symptômes locaux: otite suppurée mastoidite latente, enchifrènement, légère rougeur de la gorge.

L'impression du tableau complet de ces cas serait certes intéressant et montrerait quelle diversité de symptômes se présentaient. Un tel tableau cependant prendrait vraiment trop d'espace, puisqu'il s'agit de pas moins de 151 cas différents.

Les prises ont été faites indifféremment au nez ou à la gorge dans tous les cas où il n'y avait pas de symptômes locaux. La matière soumise à l'examen était du pus, le cas échéant, ou alors des mucosités.

EXAMENS

| | | | |
|---|---|---|---|
| Oreilles: | 30. | résultat Klebs-Loeffler positif | 21 |
| Nez : | 63. | résultat Klebs-Loeffler positif | 40 |
| Gorge : | 58. | résultat Klebs-Loeffler positif | 24 |

Soit un grand total de 151 recherches avec résultat positif dans 85 cas, soit 56.3 pour cent.

On pourrait objecter à ce chiffre étonnant que les prises nasales l'élèvent; ce qui ne serait pas étonnant lorsque l'on songe à la fréquence du coryza diphtéritique. Or sur les 63 malades dont les sécrétions nasales furent examinées, on rencontrait 19 coryzas allant du simple, écoulement peu abondant jusqu'à l'écoulement abondant de pus sanguinolent. Et sur ces 19 cas 15 donnaient une réponse positive. De sorte que les 132 cas restants nous donnent encore un pourcentage de 45.5 pour cent positifs.

Bien entendu, toutes les précautions furent prises en vue de différencier le diphtérique vrai des pseudo-diphtériques. Les examens étaient faits dans deux laboratoires différents, par M. Bolduc, au laboratoire municipal de la Cité de Montréal et par M. Gauthier au laboratoire de l'Hôtel-Dieu. Les cultures étaient faites par M. Gauthier sur milieu d'Acosta et par M. Bolduc sur milieu identique. N'étaient étiquetés diphtériques que les bacilles présentant nettement les caractères morphologiques et bio-

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logiques du Klebs-Loeffler; les douteux étant classés négatifs.

Nous sommes allés plus loin. M. Gauthier qui dans toutes ces recherches n'a épargné ni son temps ni ses soins, fit l'inoculation au cobaye avec les cultures de onze cas trouvés positifs. De ces onze cobayes, neuf mouraient dans les quarante-huit heures et l'autopsie révélait chez eux toutes les lésions de la diphtérie expérimentale soit: congestion intense généralisée, nécrose au point d'injection, *péricardite, capsules surrénales hémorragiques,* congestion pulmonaire avec foyers hémorragiques.

Il semblait donc bien que nous fussions en présence de bacilles diphtériques virulents qui chez nos petits ne déterminaient point de manifestations diphtériques classiques mais bien plutôt infection atypique. Depuis vingt mois nous n'avions eu dans nos salles aucun cas de diphtérie franche. L'examen de la gorge, qui se fait systématiquement chez tous les malades n'avait jamais montré de fausse membrane.

Nous ne pouvions pas véritablement parler d'épidémie, il s'agissait plutôt d'endémie. En effet pendant la période que durèrent les expériences la mortalité hospitalière de l'institution n'était pas plus élevée qu'à l'ordinaire et les malades chez qui furent faites les prises ne différaient en rien d'aspect d'avec ceux que nous rencontrons habituellement dans les crèches. Nous insistons sur ce point qui nous paraît très important. Rien ne nous permet de supposer que nous nous trouvions dans une période d'infection particulière. Au contraire, nous avons l'impression absolue d'être intervenu dans le cours habituel des choses. Rien ne nous avait préparé à la trouvaille d'une si grande proportion de bacillaires diphtériques.

Pour compléter le cycle de ces recherches, il nous restait à trouver la source, la voie d'entretien de cette endémie. D'enfant à enfant, médiatement, par les mains des infirmières, par les objets de literie, il y avait transmission possible. Mais il était probable qu'il se trouvait parmi le personnel des porteur de germes. Cette fois nous nous attendions à la réponse. Sur 32 membres du personnel examiné, 8 furent trouvés porteurs de germes diphtériques, soit 25 pour cent.

Enfin, comme dernière recherche, nous fimes la réaction de Schick à une vingtaine d'enfants trouvés positifs lors des dernières expériences. Les résultats cette fois furent tout-à-fait imprécis. Il y eut de nombreuses réactions douteuses; mais un seul donna une réaction franchement, nettement, positive. Il était d'ailleurs (de la série) le seul dont l'état de santé fut à ce moment profondément atteint. Il mourut peu de temps après, malgré une légère mais temporaire amélioration consécutive à l'injection de 12.000 unités de sérum. Chez lui, l'autopsie nous montra les lésions décrites tout-à-l'heure chez nos cobayes avec en plus du pus dans les deux mastoides.

Dans tout ceci nous ne prétendons pas à la nouveauté. Nous ne sommes pas les premiers à avoir trouvé des bacilles diphtériques dans la gorge, le nez, ou les oreilles de malades ne présentant aucune manifestation classique de l'infection croupale. La plus vieille édition des "Diseases of Infancy and Childhood" de Holte Holland que nous ayons entre les mains en fait mention. Dans les "Archives of Oto-Rhino-Laryngologie", Mlle. W. Drury[4] cite deux cas re diphtérie de l'oreille moyenne sans fausses membranes; de l'un de ces cas elle rapporte l'histoire à peu près superposable à celles de nos malades. En Allemagne, Kliewe et Hoffmann[5] découvrent l'existence imprévue du B. diphtérique chez 185 des 3272 nourrissons et grands enfants examinés. En février, 1927,MM. Ribadeau-Dumas et Chabrun[6] insistent sur la fréquence et l'importance de l'infection diphtérique larvée chez le nourrisson. Et que d'autres.

## CONCLUSIONS

Le récit de ces différentes recherches a été fait dans l'ordre chronologique, et nous ne voulons point en tirer des conclusions trop générales. Nous ne songeons pas à affirmer que dans toutes les crèches du monde la majorité des enfants meurent de diphtérie atypique. Nous ignorons, du moins scientifiquement, ce qui se passe ailleurs. De ce côté tout ce que nous savons c'est que dans une institution similaire à la nôtre, située dans la même région une série d'examens furent faits chez nombre d'enfants souffrant de cette rhino-pharyngite torpide apparemment bénigne que tant d'entre eux présentent. Le microscope montra une forte proportion de bacilles présentant l'apparence et les caractères du diphtérique vrai. L'hypothèse diphtérique fut-elle abandonnée comme invrai-

semblable? Nous ne savons. Mais ce qui est certain c'est que malheureusement aucune culture ni inoculation ne fut faite et les expériences ne furent pas poussées plus loin.

Dans notre clientèle privée, il nous est arrivé plusieurs fois de trouver des bacilles du croup chez des petits malades présentant des symptômes absolument banaux d'infection gastro-intestinale. Est-ce à dire que nous entendons tenir cette unique infection microbienne responsable de toutes ou presque nos morts? Pas le moins du monde. Mais il ne semble pas présomptueux après ces recherches de dire que pour nous la présence d'une telle infection spécifique, si dangereuse, et si répandue, du moins chez nous, ne peut qu'avoir une influence néfaste sur notre chiffre de mortalité. Et nous croyons que cette influence n'est pas petite.

Deuxièmement. Ce que nous voyons autour de nous empêche de croire que notre institution ait l'apanage exclusif de cette situation. Quand nous retrouvons ailleurs dans les milieux hospitaliers ou dans les foyers les mêmes symptômes, la même évolution et la même lamentable mortalité, nous croyons bien *probable* que les mêmes effets soient entrainés par de mêmes causes.

Troisièmement. Tout ce travail, couvrant une période de deux ans, nous a persuadé que le problème des crèches est un problème *infectieux* et *non pas alimentaire*. Les résultats obtenus depuis confirment absolument cette manière de voir.

Quatrièmement. Ce problème infectieux est pour nous (et vraisemblablement pour d'autres), un problème où la diphtérie clandestine est un des importants facteurs.

N.B. Nous devons en terminant rappeler encore une fois ce que nous devons à M.M. Bolduc et Gauthier, bactériologistes, et particulièrement à ce dernier dans le laboratoire duquel, à l'Hôtel-Dieu, furent faites la plupart des recherches bactériologiques.

Nous ferons une mention particulière aussi du Dr. Lécuyer, dont l'assistance et le dévouement à la Crèche d'Youville nous fut extraordinairement précieux.

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## CAUSATIVE FACTORS IN ECZEMA*

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THE diagnosis and cure of eczema is the most important dermatological problem with which we have to deal. If it is realized that eczema represents approximately 30 to 40 per cent of all dermatoses its importance both in dermatological and general practice can be readily understood.

The investigators of a decade ago held divergent views as to the etiology of eczema. Willan and Bateman, in England, believed that eczema was of both internal and external origin. In France, Biett and others stressed the underlying predisposition of the individual, and on the other hand the German and Austrian School of that time, represented by Hebra, Neumann and others, maintained that the cause was always external.

What is eczema? Highman[1] best defines it as follows: "Eczema is a catarrh of the skin possessing the pathological characteristics of an exudative inflammation. It is characterized clinically by redness, swelling, the presence of papules, vesicles, pustules, weeping, crusting and scaling in varying combinations. In its course it may be acute, subacute, chronic, and its origin depends on an interplay between various known and unknown local and predisposing causes, to which the skin lesions are reactions."

To have eczema it is required that there be an

* Paper read at meeting of Ontario Medical Association, Hamilton, May, 1929.

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eczematous or allergic disposition on the part of the skin and an irritant or exciting agent. That this disposition on the part of the skin is essential for the production of eczema is shown in the association, for instance, of scabies and eczema, for only a small percentage of cases of scabies develop eczema; the associated eczema may possibly be due to a sensitivity to biochemical products in the structure of the itch mite or its ova. Again, one may instance the influence of varicose veins in determining the site of varicose eczema. It is necessary that the individual have the eczematous disposition, for but few sufferers from mild or even marked varicosities in the leg develop eczema. There must, therefore, be as a basic factor a hypersensitive or allergic skin, in short, the eczematous individual. The underlying biological changes responsible for this allergic disposition are as yet unsolved. In this connection, Bloch[2] has shown that a normal individual may be sensitized to an external irritant, such as primula, by repeated contact with the plant. He has thus experimentally rendered the apparently normal individual hypersensitive to a specific irritant. We are not concerned here with the many types and variations of eczematous reactions. These variations depend on two prime factors: (1) the variability in the intensity of reaction on the part of the skin; (2) the grade of intensity of the etiological irritant.

Bloch,[3] of recent years, has added much to our knowledge as to causation. By applying vegetable and chemical irritants directly to the skin, such as formaldehyde, primrose, turpentine, etc., irritants that in a weak solution cause no reaction in a normal person, he has shown in a large series of cases that an eczematous reaction is produced by one or more of these irritants in 35 per cent of eczematous individuals, whereas reactions were produced by the same irritants in but 5 per cent of normal individuals. He believes from his investigations that the large majority of eczemas are of external origin, due to an underlying specific hypersensitiveness to an external irritant.

External irritants of eczematogenetic character may be of chemical, vegetable, or actinic origin. These irritants may be present in the everyday life, or may be encountered as the result of the occupation of the individual. Some forty vocations have been incriminated in this regard.

Under chemical irritants we may enumerate the various acids, alkalies, turpentine, alcohol, formalin, and a host of others. Dyestuffs are frequently incriminated as the cause of an eczema, instances of which are fur and hair dye dermatitis, which are relatively common. Under vegetable irritants may be noted the various plants which contain toxic substances which irritate the sensitive individual, such as rhus, primula, primrose, geranium, pollens, mustard, and many others. Vegetable irritants are also encountered in some occupations. Actinic radiation may very occasionally in a sensitive individual give rise to eczematous reactions. There are a whole host of external irritants in the field of everyday work which may give rise to an eczema or dermatitis venenata. The character of the reaction is usually that of a superficially acute, often intensely inflammatory, dermatitis recurring on repeated contact with the irritant. Careful questioning is needed at times, and the irritant may require prolonged search before its discovery, as in the following instance:—

CASES 1 AND 2

In 1925 two men appeared at our clinic within a short time of one another, complaining of an acute eczema of the face, thighs, legs, arms. They were dock-workers, and had been unloading a cargo of flax which had arrived from South America. They said they were accustomed to handling flax for years and had never had any previous skin eruption. After some investigation it was found that this particular cargo was very "dirty"; it was not clean flax. We procured a sample and analysis of this was kindly carried out in the Agricultural Department at Ottawa. The analysis showed that a large proportion of the chaff was made up of mustard grains. In these cases, therefore, mustard, a very strong irritant, was incriminated. These men were able, following recovery, to return to their occupations.

It has been our experience that very frequently most careful investigation and questioning fails to reveal a definite external irritant as the prime factor. At the Montreal General Hospital in a large proportion of cases of eczema of all kinds no definite proved external irritant may be found. Under chemical and vegetable irritants are many substances which are drugs. Some of these in common use are mercury, sulphur, quinine, and, indeed, many others. Mercury and sulphur not uncommonly produce an eczematous eruption

when externally applied in a hypersensitive individual, and we see in our clinic not infrequently a dermatitis venenata following the application of ung. hydrargyri ammoniati. Certain drugs, notably quinine, which is easily absorbed in the digestive tract may produce specific eczematous reactions when applied externally and also when taken by mouth, and the phenomenon of these drugs causing eczematous reactions by these two routes of contact forms a connecting link between the exogenous and endogenous origins of eczema. To cite two cases which have come under my observation and which may be of interest:—

CASE 3

A. B., aged 35, in 1925, developed an acute eczematous eruption of sudden onset over the forehead, face, ears, neck, and typical dyshidrotic eczema of the hands and feet of the small vesicular type. It was discovered that a few days previously he had been applying a frequently used hair tonic. He made a slow recovery over two or three weeks, possibly in part due to the fact that a tar lotion was prescribed for him, to which he also was sensitive. Two years later he again developed an acute eruptive eczema of the face following the application of a common face lotion. One year later a friend gave him two "C.B.Q." tablets, and within six hours he developed an acute eczema of the face with a dyshidrotic vesicular manifestation on the hands and feet. He presented an exactly similar picture to that of the first attack. Each one of these exciting agents contained quinine, and he was probably also sensitive to tar.

CASE 4

C. D., aged 40, came on account of alopecia areata of the scalp. He was somewhat under par and I gave him Syr. Hypophos. Co. In a few days he came back on account of an exudative eczema of the face, which promptly subsided on stopping the tonic. One month later he reappeared with a similar eruption on the sides of the face, and he had just prior to the outbreak applied a face lotion after shaving. Each agent again contained quinine.

Here we have a second example of a substance causing an eczema, both when taken by the mouth and absorbed in the alimentary tract and when brought into direct contact with the skin. It may be noted, in passing, that many popular scalp and face lotions are being extensively used, and I think we are seeing more and more eczematous reactions due to a specific sensitization to their ingredients, of which the commonest is quinine. It is easy to believe, therefore, that other substances besides quinine may be absorbed from the alimentary tract, and may also act as specific irritants or antigens in an eczematous individual, providing that the skin be specifically sensitized to these substances. Such substances may be classified under two headings.

(a) Substances ingested, such as various food proteins. Food proteins due to faulty digestion may be absorbed unchanged, and instances are on record where eczematous eruptions are definitely due to specific food proteins. Wheals result when the offending protein is applied to the skin. Clinical cure on removing from the diet a protein which may give a positive skin test is not, however, always obtained in adults. Occasionally, in infants, such proteins as wheat, eggs, and milk may be the cause of an eczema. The results of investigation in eczema from the standpoint of food sensitization are disappointing. Skin tests have been to me of little value in this disease, although when other investigations fail they should be carried out. It is important to remember that silk and wool sometimes act as irritants, giving rise to a patchy or generalized eczema in an infant.

(b) Partially digested food proteins; the products of bacterial action on the intermediate products of protein metabolism; and, possibly, bacteria themselves, may be classified as intestinal toxins, and it is important to remember that these are not normal metabolic products. It has been shown that many of these toxins give rise to sensitivity skin reactions, as do food proteins.[4] In a series of eczematous individuals one or more of these toxins gave rise to positive skin reactions in 16 per cent of cases as compared with only 2 per cent in non-eczematous individuals. Clinically, it is most important, in the absence of a definite external irritant, to investigate carefully the state of the alimentary tract. Constipation is most important, but, with or without constipation, the history of mild indigestion of varying degrees, associated with irregular dull headaches, ill defined malaise, is most suggestive of a toxic absorption from the lower alimentary tract, in an otherwise healthy individual. The indicanuria test is a rough guide as to the presence of a putrefactive process in the intestinal tract, and in these cases it is frequently very marked. These "toxic" cases are in my experience quite common, and the cure lies in intestinal therapy, with the exhibition of mild saline purgatives, and intestinal antiseptics, or alteratives as mercury, *B. acidophilus,* etc. The restriction of

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protein, *e.g.*, meat and eggs, in the diet is indicated in these cases, and this is a further measure which has appeared to me to be of definite value in bringing about more rapid cure of the condition.

The occurrence of eczema associated with diabetes has long been recognized, and occasionally the presence of diabetes is discovered as the result of the onset of eczema. Of recent years the disturbance of carbohydrate metabolism as a factor in the production of eczema has been more definitely investigated. The observations of McGlasson, Ayres, in the United States, and Campbell,[5] in Canada, have added to our knowledge. Dr. G. Campbell pointed out, in a series of cases observed in our clinic in Montreal, that certain eczematous persons exhibited a lowered tolerance for sugar, associated with a delay in its assimilation, as shown by laboratory blood sugar findings. He pointed out that, clinically, in patients exhibiting this disturbance, restriction of their carbohydrate intake, and particularly the sugar in the diet, was followed by cure or marked clinical improvement, such cases being frequently resistant to other measures. The importance of careful investigation regarding the ingestion of carbohydrate has more and more impressed itself on us in the past two years. In our clinic, where facilities have been made possible in the metabolism laboratory under the direction of Dr. I. M. Rabinovitch, it is a routine measure that where no definite external irritant of a chemical or vegetable origin can be incriminated a sugar tolerance test is carried out. We have been impressed with the relative frequency with which pathological variations of the blood sugar time curve have been demonstrated in our cases. It is necessary to point out here that laboratory investigations are not by any means necessary. Clinical investigation of cases frequently reveals a relatively high carbohydrate diet, and the observation of Campbell, namely, that the occurrence of eczema in an adult over forty years of age who has not before at any time been a subject of eczema is frequently intimately associated with a lowered sugar tolerance and, further, that restriction of carbohydrate, particularly sugar, in the diet is a very important factor in the cure of the condition, has been very frequently confirmed. Our investigations have further shown that younger eczematous individuals not infrequently present similar blood findings. We have recently tried to estimate in the clinic the value of these measures. Questionnaires were sent out to eczematous patients who had come to our clinic during the past four years and had exhibited a disturbed sugar tolerance. There is a certain difficulty in obtaining intelligent co-operation in clinic patients. Of 88 patients whom we investigated, the results of treatment were not obtainable in 28 cases; 16 reported that they were unchanged; and 44 cases were greatly improved or cured. A number of patients stated that following cure of their condition discontinuance of this restriction in their diet resulted in a recurrence of their eruption. The results in private practice, where more intelligent co-operation is found, and where we are able to more closely follow our patients, are very much better. An example of this may be cited.

CASE 5

D. D., aged 23, presented an exudative and scaly diffuse eczema of the neck, upper chest, flexor and extensor aspects of the arms, of three months' duration. She was anæmic and under par. There was a history of excessive ingestion of carbohydrate, and her blood sugar tests showed a lowered tolerance for sugar. There was no evidence of external irritants and no history of headaches, indigestion, constipation or other disturbance. Under a restricted carbohydrate diet, tonics, and the application of a bland ointment she rapidly improved. Three weeks after the institution of therapy, when she had considerably improved she indulged in "sweets," and promptly had a flare-up of her eczema. Following this she cleared up. Three months later, when quite normal, she again went off her diet for a period of two weeks, and she promptly had a recurrence, which cleared up under the resumption of a restricted sugar diet.

This is but one example of many such types that have been observed, and in these cases, in a clinical sense, there would appear to be a close relationship between carbohydrate consumption and eczema. Further, some cases presenting this association of a disturbed carbohydrate metabolism and eczema have presented eczemas which seemed to be very definitely associated with their occupation. We have observed some cases which under dietary measures have cleared up, and the patients have been able to return to their occupations without a recurrence of the eczema. In fact, we are finding it more and more difficult at times to make an absolute diagnosis of an occupational dermatitis without very close observation and investigation of the patient, both

from the standpoint of metabolism and a possible putrefactive process in the intestinal tract.

It is difficult to explain the relationship between certain forms of eczema and disturbance of carbohydrate metabolism. The general hypersensitiveness of the skin to external irritants is not increased, as has been shown by Usher[6] in our clinic. Possibly, as a result of the changed metabolic activity of these individuals, abnormal metabolic products or toxic substances are formed in the tissues or intestinal tract, and these in turn act as irritants. This is a possible explanation, for which, however, no proof is forthcoming. Many persons exhibit this disturbance of carbohydrate metabolism without developing eczema (there must be an eczematous disposition), and further it must be always remembered that the occurrence of eczema in these persons may be due to a definite external irritant.

The association of eczema with disturbances of the thyroid gland is also to be noted here. Occasionally one meets the association of eczema with clinical or metabolic evidences of hypothyroidism, and the exhibition of thyroid substance results in a prompt cure of the condition.

Influences such as worry, overwork, etc., may be important factors in the production of eczema, particularly in those who in their occupation are under a constant high nervous tension. No other cause, metabolic or otherwise, is to be found in these individuals, and complete change in their surrroundings is necessary to effect a cure.

May I, in summing up, quote a short paragraph from a text-book of dermatology by Erasmus Wilson, written in 1854.

"Eczema is apt to occur symptomatically, as a consequence of some constitutional disturbance or as an effect of the application of local irritants to the surface of the skin. Of the former kind are the changes that take place in the system under hygienic influences, as during the spring and summer seasons of the year, particularly when accompanied by atmospheric vicissitudes, affections of the digestion system, as dentition, the irritation produced by unsound milk in infants at the breast, and stimulating and improper food and drinks in persons of all ages. . . . .and affections of the nervous system, as mental emotions, particularly of the depressing kind. The local causes of the disease are heat and cold, together with friction and irritation of the skin produced by whatever cause. Thus occasionally we find eczema resulting from the sun's rays, a variety which has by Willan been denominated eczema solare. It not infrequently attends the inflammation produced on the skin by the irritation of a blister, or by the application of the compound sulphur ointment or a Burgundy pitch plaster."

These observations, which were founded on clinical observations and clinical investigation, are still to-day essentially sound. We have progressed in our more exact knowledge of eczema in recent years. Ringworm, yeast, and coccal infections of the skin giving rise to eczema-like reactions, have been differentiated and taken out of the field of eczema. There is no one cause for eczema. The common factor in all eczematous individuals is an underlying hypersensitivity on the part of the skin, and, granted this disposition, a legion of internal or external irritants may be exciting agents. The specific reaction of the skin to external irritants, the factor of alimentary toxins, and the significance of the diet as it pertains to carbohydrate and protein metabolism, represent, I believe, the more important aspects in the investigation of the eczematous individual.

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Medicine is not wholly materialistic: it would discharge its functions sadly if it had nothing in view but a healthy body. Let us have that by all means if we may, but if we cannot let us bear in mind that comfort and cheerfulness do many people good besides the sick man. When prevention and cure have failed, there is much left to do which is worth doing.—*The Lancet.*

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# SEX HORMONES OF THE FEMALE*

## A REVIEW

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SINCE the pioneer work of Berthold (1849) in demonstrating the internal secretory function of the male gonad in regard to the maintenance of secondary "sex stigmata" in birds, great advances have been made in the field of sex physiology. It has been within the last decade, however, that outstanding progress has been made in the development of this special field. It is the purpose of this article to outline, as briefly as possible, the present status of our knowledge concerning the endocrine aspect of this subject as it relates to the female. In a field where theory is so rife, it is essential that one should endeavour to keep theory and facts apart, and in the following paragraphs an earnest attempt has been made in this direction.

The earliest manifestation of endocrine activity of the gonad is found in the young rapidly differentiating and developing embryo. From the earliest elements of the Müllerian and Wolffian duct systems are developed the female and male gonad respectively. The gonad, male or female, as the case may be, proceeds, it is believed, to influence somatic development of the embryo and later of the fetus, so that even at birth certain sex characteristics are well developed. The further development and accentuation of the secondary sex qualities reaching a climax at puberty are so well known and accepted as evidences of gonadal hormone functioning that they may be dismissed at once from this discussion.

A more detailed survey of hormonal factors playing a part in sex physiology of the female may be described under the following heads: (1) the ovary; (2) the pituitary gland; (3) the placenta.

* Read at a meeting of the Sigma Xi Society, McGill University, December 18, 1929.

### THE OVARY

Marshall and Jolly,[11] as early as 1906, demonstrated that the ovary produces a hormone which causes the phenomenon of œstrus. Subsequent workers — Adler,[1] Iscovesco,[8] Fellner,[5] Hermann,[7] Frank[6] and others — extended and amplified this observation. Allen and Doisy,[2] in 1923, developed an accurate method of biological assay of the ovarian hormone of œstrus, best known now as œstrin. They made extracts from pure follicular fluid, and by use of the vaginal smear method were enabled to test their product as they proceeded with its concentration and purification. They found, as did Iscovesco, that the "activity" of ovarian extracts in regard to the production of œstrus in castrated females was associated with the ether soluble or lipoid fraction, and with their new method of assay as a guide they were able to produce very concentrated extracts.

Frank, who has worked in the field for a number of years, has recently written a monograph on the "Female sex hormone", by which title he prefers to designate the hormone of œstrus. An excellent review of the literature, both laboratory and clinical, is given in this text. An even more recent monograph by Parkes[13] covers the subject most exhaustively.

Œstrin has been demonstrated elsewhere than in the ovary. Of chief interest in this connection is its occurrence in the placenta, in amniotic fluid, and in the blood and urine during pregnancy.

The physiological properties of œstrin are best manifested by injecting the hormone into a castrated adult female rat. Forty-eight hours thereafter the animal is found to be in a state of full œstrus as shown by its behaviour towards the male and by the flush of cornified epithelium in the vaginal smear. If the animal is sacrificed

marked hypertrophy of the vagina and hyperæmia and distension of the uterus will be noted. Prolonged treatment with œstrin injections is said to cause enlargement of the breasts and even the secretion of milk subsequent to the withdrawal of the treatment. Stimulation of milk secretion is denied by some workers. The effect on the male is probably anti-masculine in the main, but the hypertrophy of breast tissue in male guinea pigs has been noted.

If œstrin is injected into young and immature rats or mice the phenomenon of œstrus is induced as it is in the castrate, also the same effect is obtained in the öophorectomized immature animal. A point of great interest in the physiology of œstrin is its *apparent non-effect upon the intact normal ovary.* The injection of œstrin during pregnancy results in abortion if the dosage administered be adequate. The amount required in the later stages is much greater. Œstrus may also be induced by œstrin in the lactating animal. It is claimed that œstrus changes may be induced in the senile animal by injection of the hormone. The ovary, however, is not stimulated and ovulation does not occur.

### THE PITUITARY GLAND

It is apparent that since the hypertrophy of the genital tract at each period of œstrus is due to a specific stimulus afforded through the functioning of the hormone œstrin, the ovary must liberate this internal secretion at periodic intervals. The question therefore arises as to what controls the periodicity of the ovary in this one respect at least. This question has been largely answered by the conclusive demonstration in the work of Smith and Engle,[14] and Zondek and Aschheim[17] that the phenomenon of ovulation is in large measure controlled by the secretion of the anterior lobe of the pituitary gland. The question as to how the pituitary gland functions as it does remains for the present unanswered.

Smith and Engle, and Zondek and Aschheim, by means of fresh intramuscular implants of anterior pituitary substance, succeeded in demonstrating intense stimulation of the immature ovary of rats and mice. The effect consisted in marked hypertrophy of the infantile gland due to the rapid growth of Graafian follicles. The development of the follicles appeared to follow a normal course, and normal but superovulation resulted. But of even greater interest was the production of premature puberty and all the phenomenon of œstrus, opening of the vagina, cornification of the vaginal mucous membrane, enlargement, engorgement and distension of the uterus. This latter result was undoubtedly due to the liberation of œstrin from the ovaries of the immature animal, stimulated to activity by the anterior pituitary hormone.

The recent experiments of Parkes[13] in which follicular ablation was produced by means of x-rays supply evidence that the periodicity of œstrus is not necessarily governed by the periodic maturation of follicles.

Further evidence that the pituitary gland has a profound influence on the gonad is found in the results of hypophysectomy. Removal of the hypophysis causes cessation of ovarian development and activity.

If one considers the normal ovarian cycle (maturation of the Graafian follicle resulting in rupture and escape of the ovum, to be followed immediately by the development of the corpus luteum from the old follicle) and the subsequent history of the corpus luteum, depending as it does on the fate of the shed ovum, one sees presumptive evidence, at least, of endocrine activity other than that thus far discussed. Many of the presumptive functions of the corpora lutea have of late years been definitely proved as entities. Functioning corpora lutea have been shown to inhibit ovulation and œstrus changes in the genital tract. The recent work of Corner[3] has demonstrated that the progestational proliferation of the uterine mucosa is a function of the corpus luteum and he has succeeded in producing this effect by means of extracts. He has also shown the importance of the corpus luteum in maintaining the nutrition of the uterus of the impregnated animal by carrying rabbits through pregnancy which had been öophorectomized following impregnation.

The development of the mammary glands from the condition in which they are found at œstrus to that at the end of the luteal phase is another function of the "yellow body".

Since there is a great deal of species difference in regard to the phenomena of sex, it is rather difficult to correlate the conditions as found in the human female with the œstrus cycle as manifested in the various lower species. For example, ovulation and œstrus are as a rule

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synchronized in the lower animals, whereas in the human individual ovulation has been abundantly proved to be an inter-menstrual phenomenon occurring probably on the fourteenth day following the beginning of the last menses. The rabbit and ferret only ovulate following copulation or mechanical stimulation of the cervix. Immediately following ovulation in these species, the corpora lutea develop, and as the life time of the corpora is, in the absence of impregnation in the rabbit, about two weeks, the condition of pseudo-pregnancy can be studied to advantage here. Pseudo-pregnancy is apparently entirely a corpus luteum phenomenon. It consists, in the rabbit, of considerable mammary gland and uterine hypertrophy. It also represents a period of sensitization of the uterus because mechanical irritation, as from a foreign body introduced into the uterus, leads to the formation of a tumour-like growth, the deciduomata first described by Loeb.[9]

Following atresia of the corpora lutea retrogressive changes in the mammary gland and uterus occur. Reasoning from such observations it has been suggested that menstruation, which is so markedly a human characteristic, is really the termination of what might be termed a pseudo-pregnant condition, due to atresia of the corpus luteum which develops and flourishes for ten or twelve days following ovulation. In support of this theory there is the evidence that removal of a fresh corpus luteum is followed very shortly by the menstrual flow. Marshall[10] has suggested that menstruation represents pseudo-pregnancy and pro-œstrus degeneration telescoped into one.

There is a certain amount of evidence that the anterior lobe of the pituitary gland may produce a second hormone which has an inhibitory effect upon the ovary. Evans[4] found that the injection of his alkaline extract of the anterior lobe, which contains the growth principle, caused rat ovaries to become almost completely luteinized with concomitant cessation of periods of œstrus. Teel,[15] by injecting a similar extract during pregnancy, was able in the rat to prolong the gestation period from two to six days beyond the normal. Wiesner[16] also claims that there is a second and inhibitory factor in the anterior pituitary and also in the placenta, which induces luteinization of follicles and a pseudo-pregnancy reaction in the uterus and vagina.

### THE PLACENTA

Zondek and Aschheim found that implants of placenta produced similar effects to anterior pituitary implants or injection of anterior pituitary emulsion. They also found that the urine of pregnant women which had been freed from œstrin by extraction with ether contained anterior pituitary hormone. Similarly, the blood during pregnancy has been shown by them to produce an anterior pituitary effect when injected into ammature mice. Wiesner[16] has worked extensively with placental extracts, and claims the coexistence of two hormones therein, one stimulatory to the ovary, the other causing inhibition of œstrus and a pseudo-pregnancy reaction. The placenta is therefore rich in two hormones—œstrin; a pituitary-like ovarian stimulant; and, possibly, a third inhibitory principle.

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# THE OVARY-STIMULATING HORMONE OF THE PLACENTA

PRELIMINARY PAPER

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IT has been abundantly proved that the placenta contains the hormone of œstrus. This hormone, "œstrin", or the "female sex hormone", as it is designated by Frank,[5] was first studied in detail by Allen and Doisy.[1] They developed a method for the accurate biological assay of extracts containing the active principle. The assay is dependent on the characteristic property of the hormone to produce the phenomenon of œstrus in a fully castrated female rat. Since their original work on follicular fluid as a source of this œstrus-producing ovarian hormone, œstrin has been abundantly demonstrated elsewhere than in the ovary. Placenta, amniotic fluid, and the urine of pregnancy have been shown to contain very considerable amounts of the hormone.

Prior to the development of more accurate methods of assaying for œstrin, many earlier workers had proved that lipoidal extracts of placenta when injected into young females caused premature maturity of the uterus and vagina. A similar result was obtained with adult castrates.

Since œstrin is most readily obtained by taking advantage of the fact that it is freely soluble in fat solvents, and can be removed completely from aqueous suspension by the use of ether, workers in this field have for the most part confined their investigations to the lipoid fraction of tissues or fluids studied. The demonstration that a water-soluble hormone having physiological properties quite distinct from œstrin may occur separate from or in conjunction with the latter is an outcome of the independent work of Smith and Engle[9] and of Zondek and Aschheim[11] on the ovary-stimulating action of implants of anterior pituitary substance. These investigators were able to show the most dramatic results in immature female rats and mice following the intramuscular injection of fresh anterior pituitary gland or saline suspensions of the same. The effect of such treatment is to cause a most rapid development of the immature ovary. Smith and Engle report that the ovary of the experimental rat may be ten-fold the size of that of the control, and nineteen-fold in the case of the treated immature mouse. The increase in ovarian tissue thus produced is due for the most part to the rapid maturing of Graafian follicles. These apparently mature in a normal manner and superovulation results. But even of greater interest is the fact that as a result of the stimulation of ovarian activity, œstrin is liberated, producing its typical effects, *viz:* hypertrophy of the genital tract and the phenomenon of œstrus. The work of these authors has therefore established that a hormone of the anterior pituitary gland can cause by direct stimulation of the ovary (liberating œstrin) all the effects of œstrin *per se*. There is this sharp distinction between the anterior pituitary principle and œstrin—anterior pituitary hormone has no effect on the castrate, whereas œstrin acts just as effectively in the castrate as in the normal female.

Zondek and Aschheim later demonstrated that implants of 0.1 grm. of placenta produced ovulation in immature mice. Blood serum and the urine of pregnancy were found to be similarly active, in doses of 0.5 and 1 to 2 c.c. respectively. They have also detected the ovarian stimulating principle in decidua, in the corpus luteum of pregnancy, in tubal mucous membrane, and in the blood of the new-born. They have prepared an œstrin-free product from the urine of pregnancy and have developed a method of biological assay of the principle dependent upon the production of hæmorrhagic follicles in the ovaries of 6 to 8 grm. immature mice. The pioneer work of Smith and Engle, and of Zondek and Aschheim, on the ovary-stimulating hormone of

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the anterior pituitary gland has been confirmed by Fels,[4] Brouha and Simonnet,[3] Loewe,[6] and Siegmund.[7]

Dr. Wiesner,[10] of the Department of Animal Breeding of Edinburgh University, has recently succeeded in preparing potent aqueous extracts of the ovary-stimulating hormone from human placentæ. Wiesner's method consists in extracting the fresh placenta or placental press-juice with sulphosalicylic acid. This has the advantage of giving almost immediately a practically protein-free extract, which, after neutralization and clarifying by adequate filtration, may be injected directly. It has the disadvantage, however, that it still contains sulphosalicylic acid, or its salts, and does not readily lend itself to concentration processes. Dr. Wiesner visited the writer's laboratory in September, 1929, and demonstrated in a single but convincing experiment the effectiveness of the sulphosalicylic acid extract of fresh human placenta in producing premature maturity in the young rat. At Dr. Wiesner's very urgent request the writer took up the problem of the concentration of the premature maturity producing principle in the placental extract. A considerable number of experiments were therefore undertaken with sulphosalicylic acid extract of placenta and Dr. Wiesner's claims for the effectiveness of this extract were amply confirmed. At times, an immature female rat could be made to develop full œstrus and ovarian hypertrophy (confirmed by microscopic sections) on the fifth day following the injections of an amount of extract equivalent to 1/3 grm. of placenta. It was found best in practice to give two injections, one on the first and one on the second day, and to sacrifice the test rat on the fifth day.

It soon became apparent that the presence of the sulphosalicylic acid in the extract presented a most formidable barrier to further concentration and purification of the active principle. A variety of methods of extraction and fractionation were therefore resorted to and as a result it has been found possible to attain great concentration of the active principle. It has been obtained free from protein, salt, lipoid and œstrin, and in the form of an aqueous solution it may be administered either subcutaneously or orally. It is possible to place the equivalent of 100 grm. of placenta in 1 c.c. of water with a relatively small loss of the active principle contained in the original tissue. The potency of any extract may be ascertained fairly accurately in terms of rat units by making use of the slightly modified method of Zondek and Aschheim referred to above. The minimal amount given in two injections on successive days to produce full œstrus in immature rats three to five weeks old on the fifth day may be taken as the unit. It is also essential that the extract should be without effect on castrates.

Whether, as it has apparently been assumed, the ovary-stimulating hormone which has been demonstrated in anterior pituitary implants, in anterior pituitary extracts, in the blood and urine of pregnant women, and in the placenta, is the same in each instance remains for the present an academic issue. Why the pituitary gland should liberate this secretion so promiscuously during pregnancy, so that tens of thousands of rat units are lost in the urine, and why the placenta should act as a storehouse, are questions which must remain unanswered for the present. The writer prefers to hold the theory that in the case of the placenta the hormone with which we are dealing is actually elaborated therein.

Smith[8] has stated that anterior pituitary gland is ineffective by the oral route. A chance laboratory technical error gave a clue to the fact, later established, that the placental hormone under course of study was quite effective when administered by mouth. Certain control immature animals which were caged with injected animals were observed to show œstrus. Since there is nearly always an appreciable leakage of the injected fluid at the point of injection, and as rats are very prone to lick one another's coats, it seemed that this was the obvious explanation for the observed result in this case. Systematic feeding experiments were carried out. It was found best to administer the extract by mixing it with finely ground lean meat, which absorbs it almost completely, and which the animals eat ravenously. The amount of extract thus effective was surprisingly small. The equivalent of one gram of fresh placenta fed daily as an aqueous œstrin-free extract has produced œstrus on the fifth day. Much larger amounts produce the same effect.

In order to ensure the conviction that the efficiency was unimpaired by digestive juices, the œstrin-free extract has been treated with gastric

juice of known peptic activity for as long as seventeen hours. No loss of potency was observed. Similar results were also obtained after tryptic digestion during a period of two hours.

The results obtained by oral administration and the digestion experiments outlined above would seem to indicate one of two things—either the placental ovary-stimulating hormone is essentially different from that of the anterior pituitary, or the latter has not as yet been obtained in a sufficiently concentrated form to show similar properties.

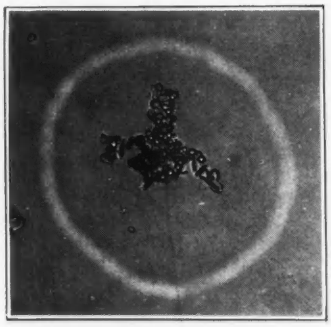

FIG. 1.—Photomicrograph of a potent crystalline fraction.

In order to study adequately the ovary-stimulating factor in placenta, it is necessary to employ a very large white rat or mouse colony. The albino rat has been used almost exclusively in this work, and breeding has been so arranged that litters of immature females of three to four weeks of age are available at all times. It is essential that both the breeding stock and the young be exceptionally well nourished. This is assured by feeding the basic diet of Sherman (whole wheat flour two parts, and powdered whole milk one part), supplemented by brewer's yeast, wheat germ, and a liberal amount of raw, lean meat.

A brief account of the more important findings to date in this research will now be given.

1. Immature female rats from 35 to 60 grm. in weight, and from 3 to 5 weeks of age, have been used according to a slightly modified technique of Aschheim and Zondek and of Wiesner, to assay biologically the content of the ovary-activating hormone in placental extracts. This method of assay has made possible the concentration and purification of the active principle by means of fractionation processes, to be described at a later date, to the point where one rat unit may be represented by 0.01 mgm. of dry substance. Certain micro-crystalline fractions of great potency have been obtained, but it is impossible to state as yet whether such fractions are pure chemicals. It is of special interest that immature white rats thus stimulated by the placental hormone to a state of œstrus as a rule become cyclic. Nine of these have also been impregnated by an active male in a normal manner.

FIG. 2.—Genital tract of rat injected at 27 days of age with a total of 2 c.c. of an extract made from the crystalline fraction shown in Fig. 1. Autopsy on fifth day.

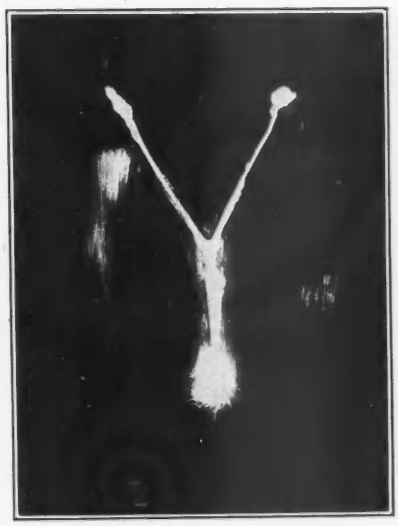

FIG. 3.—Control for Fig. 2.

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If injected immature rats are sacrificed at various periods following the administration of the hormone, one notes first the rapid development of the Graafian follicles, associated with the changes in the mucous membrane of the vagina leading up to the œstrus desquamation of cornified epithelium. Corpora lutea then appear and one finds that the vaginal mucous membrane has now changed from the squamous to the cuboidal cell type. In our experience corpora lutea are not found in the ovaries of immature control rats. It is possible, therefore, to substitute the finding of corpora lutea in the ovary of immature animals injected with the placental hormone for the well-known œstrus phenomena usually made use of in biological testing. When the appearance of young corpora lutea is made the basis of a positive reaction the test animal may be sacrificed on the sixth or seventh day following the injection, or even later. It is possible, however, to have corpora lutea appear earlier, since a positive vaginal smear may on occasion be noted as early as the third day.

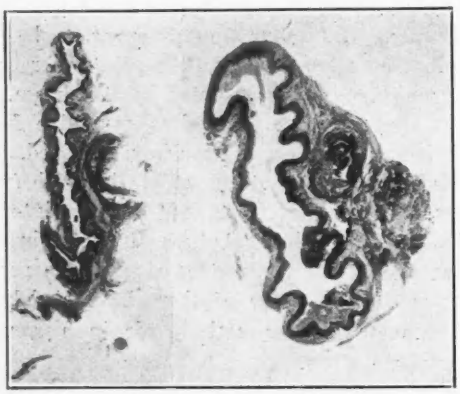

FIG. 4. — Cross section of vagina of immature rat.



FIG. 5.—Cross section of vagina of immature rat treated with placental hormone.

2. It has been shown that the same physiological effects may be produced in immature rats by oral administration of the hormone as by subcutaneous injection. The dosage by mouth necessary to produce these effects may not be more than two or three times the effective subcutaneous dose.

3. The hormone has been shown to be effective after moderate periods of exposure to the action of the digestive enzymes, pepsin and trypsin.

4. Injection of the active extract into adult castrates over a period of weeks is without effect. Injection of adult but vigorous normal females with two rat units daily has had very little effect on the normal œstrus cycle. In these experiments the animals were first submitted to a control period during which, by the taking of daily vaginal smears, the individual cycles were established. Œstrus occurs in most adult animals at regular intervals of four to six days. Apart from a slight extension of the period of cornification of the vaginal epithelium no effect was noted. Two pregnant animals receiving similar dosage daily, carried through a normal pregnancy, labour and lactation period, and, even though the injections were continued bi-daily, the animals again became pregnant following the introduction of a vigorous male, and a second time delivered a normal litter in the normal time. One would anticipate in the light of Smith's work, in which he caused termination of pregnancy in rats by pituitary transplants, that abortion might be induced by the above treatment. This may be a matter of dosage and the experiments are being repeated, using much larger doses in terms of rat units.

The injection of 12 rat units daily for three weeks produced no ill effect in a 2-kilo rabbit, and no marked change in the chemical constitution of the blood, apart from a slight increase in cholesterol.

5. The laboratory investigation making possible the production of a standardized extract containing the ovary-stimulating hormone factor, and its physiological effects having been studied in sufficient detail in certain animals, seemed to justify the view that clinical investigation of the effectiveness of the extract might now be started. On *a priori* grounds one may reason that only those individuals who give definite evidence of hypoactivity of the ovary may be expected to receive benefit by the placental hormone. Therefore, in an experimental clinical study only such types of cases should be treated. Dr. A. D. Campbell is collaborating in this work and already a few typical patients with hypo ovarian signs and symptoms have been placed under treatment. The results so far obtained have been encouraging. (See the following paper in this issue).

One must remember that luteinization of the ovary has been produced by certain alkaline

pituitary gland extracts, furthermore that Wiesner has demonstrated luteinization following injection of his placental extract. It is possible, therefore, that overdosage might in the end result in sterilization, due to excessive lutein formation. For this reason, any clinical trials must necessarily be carried on with the greatest caution.

6. The laboratory results reported in this preliminary communication are based on assay studies of 150 immature rats, as well as on 12 digestion experiments and 9 feeding experiments. Upwards of 500 microscopic preparations have been made and examined.

It is a great pleasure to acknowledge the kindly interest and co-operation of Prof. W. W. Chipman, and to thank him for placing the material of the Royal Victoria Maternity Hospital at our disposal. Our thanks are also due to Dr. S. Langevin and the Sisters of the Misericordia Hospital for kindly supplying material.

We wish especially to thank Dr. Wiesner for bringing the problem to this laboratory for investigation.

We also desire to acknowledge the most valuable technical assistance of Mr. M. McPhail, of Miss J. Williamson, and of Mr. A. A. Long. We are also indebted to Professor F. E. Lloyd for assistance with the photography.

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# ON THE CLINICAL USE OF THE OVARY-STIMULATING HORMONE OF THE PLACENTA

## PRELIMINARY REPORT

BY A. D. CAMPBELL, AND J. B. COLLIP,

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SINCE it has been shown* that the "ovary-stimulating hormone of the placenta" has a specific effect in activating the ovary of the immature rodent, it has been deemed advisable also to carry out clinical experiments with this substance. These experiments obviously demanded great caution, and every care was taken in carrying them out.

Selected cases of ovarian hypofunction were therefore placed under treatment by oral administration of the extract. At first a very small dose was given, but it was soon discovered that the dosage could be greatly increased.

It is too early to make a definite pronouncement upon the value of this treatment, for numerous clinical factors have yet to be considered, as well as the question of dosage and duration of administration. It may be said, however, that definite results of a most encouraging character have been obtained in five cases of oligo-menorrhœa, in two cases manifesting distressing menopausal symptoms, and in two cases of dysmenorrhœa.

The following case reports are submitted from this series.

### CASE 1

A girl, unmarried, Canadian, aged 17, who complained of amenorrhœa for three years.

*Personal history.*—Menstruation had begun at the age of 14, appearing as a slight "spotting" on two occasions within the first year, at intervals of four months. For the past two years she had had so-called nocturnal epilepsy, but there had been no headache, no symptoms of indigestion or constipation, no pelvic pain, and no leucorrhœa.

*General examination.*—She was of an exceedingly well developed athletic type. The integumentary and glandular systems were negative. The general distribu-

* See this issue, page 215.

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tion of hair was normal. The eye grounds were normal. X-ray examination of the skull showed a normal sella turcica.

*Pelvic examination.*—The hair on the vulva was rather sparse; the perinæum was non-scaphoid; the hymen was intact. Rectal examination showed the uterus to be small, and of normal shape and position. The cervix was small and rather long.

*Treatment.*—On November 30, 1929, a dilute extract of placenta was administered by mouth. This was gradually increased. In all, 500 rat units were given. It was discontinued on December 22nd, on which date menstruation began, lasting four days, with no pain or vomiting or other untoward symptoms. Menstruation reappeared spontaneously on January 17, 1930, lasting four to five days, and being associated with no untoward symptoms. She had received no extract since December 22nd.

### CASE 2

A Canadian, married, aged 26, complaining of nervousness, loss of weight, and comparative amenorrhœa.

*Personal history.*—She had had a curettage after abortion one year ago, during the second month of gestation, since which time the menses had become scanty, lasting only part of a day.

Menstruation had begun at the age of 13, and was of the four-day type, occurring every 28 days, and causing no special symptoms. Her personal history contained nothing of importance.

*Physical examination,* on December 14, 1929, showed her to be thin and nervous, weighing 119 lbs., and showing signs of early but acute hyperthyroidism. Her basal metabolic rate was +29. The general physical examination was otherwise negative.

*Pelvic examination.*—Vagina marital; cervix normal; uterus small and hard.

*Treatment.*—On December 14th she was given five c.c. of the extract by mouth, three times daily (one c.c. is equal to five rat units). On January 11, 1930, she menstruated three full days. On January 17th the extract was discontinued. On January 29th the basal metabolic rate was found to be +1. Her weight was now 127 lbs., and her nervous symptoms had disappeared.

### CASE 3

A Canadian, unmarried, aged 28, complaining of dysmenorrhœa.

*Personal history.*—She had had scarlet fever at the age of five, measles at ten, and influenza at 16. Appendectomy had been performed at 18.

Menstruation had begun at the age of 13½ years, and appeared regularly every 28 days. It was accompanied each time by intense abdominal pain, at times necessitating a sedative for relief. Vomiting also accompanied each epoch.

*Physical examination.*—She was of excellent physique, and the general examination was negative.

*Pelvic examination.*—Rectal examination showed the hymen to be intact and the cervix to be normal in length. The uterus was acutely anteflexed. Her last menstrual period had been December 26, 1929.

*Treatment.*—On January 9, 1930, she was given the extract by mouth; 75 rat units were administered daily for eight days. She menstruated from January 20th to the 25th, and for the first time in her life the menstruation was not accompanied by either pain or vomiting.

During the course of treatment certain patients have manifested symptoms of nausea, whilst others experienced some discomfort in the pelvic region. Others stated that they had experienced dreams of a vivid and unusual character. Severe headache and mental depression have also occurred. As a rule the patients voluntarily expressed a feeling of well-being in from four to five days after withdrawal of the extract.

It is interesting to note that in view of the well established fact that the extract is without effect on the öophorectomized rodent, clinically, one cannot expect relief from menopausal symptoms after pan-hysterectomy. One such case was studied, with the anticipated failure to obtain any beneficial results.

### COMMENT

The suggestive results obtained in this small group of cases have encouraged us to continue the experiments in the clinical use of this hormone on a more elaborate scale. Our experience thus far has demonstrated that patients should be selected, hospitalized and thoroughly investigated before and during the administration of this percental extract. A detailed report of such clinical studies will be made at a later date.

It is hoped that such studies will throw new light upon the problems of ovarian dysfunction and hyperthyroidism; and in addition, that the study of the ovary-stimulating hormone in the blood, and its distribution in the placenta of both the normal and the toxæmic pregnant woman, will help to unmask the etiology of certain of the so-called toxæmias of pregnancy.

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REVOCABLE STERILIZATION OF THE FEMALE.—Haberlandt since 1919, has been experimenting on the problem of producing temporary sterility in female animals. Subcutaneous transplantation of ovaries from pregnant rabbits and guinea-pigs produced temporary sterility in these. The effect is thought to be brought on by the formation of a hormone in the transplanted corpus luteum, which inhibits follicle maturation. After resorption of the transplanted ovaries the animals became pregnant and gave birth to mature, normally developed, living young. Sterility could be obtained for two to three months. Haberlandt obtained identical results by the daily subcutaneous injection of certain ovarian and placental extracts on the market. He is convinced of a hormonal action in securing temporary sterility in these animals. It is not inconceivable, therefore, that, when we know more of ovarian hormones and when ovarian extracts are really active, Haberlandt's work on animals may be of practical value in producing the temporary or revocable sterilization of women—*Zentralbl. f. Gynäk.* **51:** 1418, 1927.

# HYPERTROPHY OF THE PROSTATE*

BY JOHN R. PARRY, B.A., M.B.,

*Hamilton*

IN reducing the mortality from operations there are three important factors: first, early diagnosis and consequently early operation; secondly, the preparation of the patient so as to be in the best possible physical condition for operation; thirdly, improvement in the technique of the operation itself. Twenty years ago, the mortality from the operation for hypertrophy of the prostate was from 25 to 50 per cent; to-day the mortality is from 2 to 6 per cent. The profession may well be proud of this when one considers that the ages of the patients are between 55 and 90, with an average age of 65, certainly not an ideal age for operations.

Owing to the low mortality and the good functional results, the operation is much more frequently done than even five years ago. The number of prostatectomies performed in the city of Hamilton in 1928 was double that in 1924. No longer does the general practitioner tell these men that they are too old to have an operation. In simple hypertrophy I have only refused operation in one patient referred to me, as in that case the phenolsulphonepthalein output was practically nil. Another consideration is the very high percentage in which carcinoma develops, fully 20 per cent, and this factor should encourage the general practitioner to advocate early operation.

The early symptoms are mild in character. The patient is suffering only slightly but realizes there is something wrong with his urinary apparatus. There is only moderate frequency of urination, usually worse at night. The stream is slow in starting and sluggish. Such patients are in good physical condition. Their cardiovascular systems have not become affected; there has been no kidney damage, and no infection of the bladder. On examination per rectum, a moderately enlarged, soft, smooth prostate may be palpated. Of course these factors are not sufficient to advise operation. Further examination must be made. Has this man any residual urine? After voiding, a bicoudé catheter is passed, and the amount of residual urine is shown. A cystoscopic examination is then made, and if nothing more than an enlarged prostate is found operation is indicated. Should there be residual urine, without enlargement of the prostate as felt per rectum, and none seen in the bladder with the cystoscope, how then should one interpret the findings? Not many years ago, every elderly man who had urinary disturbance was assumed to have an enlarged prostate, and when his physician found residual urine no doubt about the enlargement existed. Simple benign prostatic enlargement meant obstruction and obstruction meant hypertrophy. When palpation revealed a small, apparently inoffensive prostate it was concluded there must be certain protrusions into the bladder—middle lobes—to cause the disturbance. Often such was found to be the case, but quite frequently absolutely no enlargement was seen with the cystoscope; that is, some persons having all the subjective symptoms of hypertrophy had no hypertrophy. The neck of the bladder was the offender. At operation the introduction of the finger disclosed at once a tight ring which is absent in the normal sphincter. The exact nature of this median bar is still uncertain. Sclerosis is not always present, spasm and hypertonicity play a part. (Section of the ring in any place often causes its disappearance, as also does fulgurizing or a V-shaped excision.) Some authorities place the frequency of this median bar as high as 20 per cent, but in my own experience it has not been more than 5 per cent.

Provided then a diagnosis of simple hypertrophy of the prostate with consequent residual urine has been made, what treatment is indicated? With the patient in good physical condition, without kidney damage, without any affection of the cardio-vascular system, and without cystitis, the case a couple of years ago would have been considered ideal for operation, and a prostatectomy would have been done

* Paper presented at the annual meeting of the Ontario Medical Association, Hamilton, May, 1929.

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forthwith. It would come as a great shock to the surgeon should this type of case die from infection. But this is what occasionally happened. We know now that even these very early cases, who are in such good physical condition, should be hospitalized for a week or ten days, a catheter passed twice daily, and the bladder irrigated, in order to create a certain amount of immunity or resistance. If this is done there should be practically no mortality from the operation. However, more than 90 per cent of the cases that come to operation do not come in this stage. Most of them come with infected bladders, and they are all more or less familiar with the catheter. Often, apart from instrumentation, there is bleeding of larger or smaller amounts. Kidney damage as a result of back pressure is present, as shown by dry tongue, rapid pulse, disturbed cardio-vascular system, headaches, loss of appetite, pallor and feeling of malaise. The blood chemistry tests will show urea-nitrogen 60-100, creatinin 3-5; and the white count is often 12,000-18,000. The amount of residual urine may be 10 ounces, or there may be complete retention.

What then is the treatment of these advanced cases? Twenty years ago they were sent into the hospital and operated upon the next day, or even the same day. The mortality was almost prohibitive. When it was realized that neither acute retention, nor a cystitis so severe that the patient could stand it no longer, nor the inability to further use the catheter, was an indication for immediate operation, the mortality immediately improved. It was then that the operation became divided into two stages, *viz.*, a preliminary cystotomy under gas or local anæsthesia; later, when the cystitis had become less, the kidney function restored, and the cardio-vascular system improved, the operation was completed. Now in this way the two largest factors in the mortality were almost eliminated, viz., uræmia and sepsis. There still remained the trouble with hæmorrhage. Various means were tried. The cavity was packed with gauze and this was allowed to remain in for three to seven days, and certainly this was a help. Then the different types of rubber bags were tried, and are still being used. It became apparent that the first essential was to stop as far as possible all bleeding before the patient left the operating table. Bleeding points were ligated, tags removed, and often a running suture was passed around the prostatic bed. It was found that it was difficult to expose those cases that had been drained for a considerable time, owing to contraction and adhesions of the bladder, whereas in the clean cases, where a primary prostatectomy was done, exposure was much more easy. With the indwelling catheter more than 80 per cent of cases can be prepared for prostatectomy without the preliminary cystotomy. As a matter of fact, the cystotomy itself was not without danger, and there followed a considerable mortality from uræmia. With the use of the indwelling catheter one can improve the cystitis, and repair the kidney damage just as well as by cystotomy. About 6 per cent do not tolerate the catheter, 10 per cent have calculi, and 3 per cent diverticula, and in these cases one still resorts to the two-stage operation. Since January, 1927, I have used the one-stage operation in more than 90 per cent of cases. In using the catheter too much stress cannot be laid upon the importance of not completely emptying the bladder at the first sitting. The complete removal of all back pressure upon the kidney results in congestion of the kidneys and possibly complete suppression. With the indwelling catheter, within two to four weeks, the majority of this group of cases may be made ready for operation.

The observations presented in this paper are based on a study of the last 100 cases under my care. There was a mortality of 6 per cent. All operations have been suprapubic. Since January, 1927, there have been 35 cases with one death, and these have all been done with one exception in one stage.

### PRE-OPERATIVE TREATMENT

The patient now is not considered in condition for operation, unless he feels well, eats well, sleeps well and looks well. It is surprising how quickly the change from a sick man to a well man often takes place. As soon as he is admitted to the hospital, either a soft rubber or a bicoudé catheter is passed and fastened with adhesive plaster about the penis. This may require for a couple of days a few doses of codeine (½ grain hypodermically) in order to relieve the irritation of the catheter. After the second day the majority find no discomfort from its presence. Sodium acid phosphate and

urotropin are given four times daily. The bladder is irrigated three times a day with 1-3000 acriflavine. The patient is encouraged to drink large quantities of water, a pitcher and glass being kept constantly at his bed side. If he is fond of buttermilk that also is given in large amounts. The bowels are kept fairly loose with a morning saline. After a few days the tongue begins to clear, and the appetite improves. In cases where the cardiovascular system is affected, the patient is then digitalized. It is never sufficient in these cases to have merely a normal blood chemistry test or even a normal phenolsulphonepthalein output. As stated above, as soon as the patient feels well, eats, sleeps, and looks well, you may be sure that the blood chemistry and pthalein output will be satisfactory. The average period of preparation in the last 35 cases (where the one-stage operation was done in 34 cases) was 11½ days. The one in whom a two stage operation was done was a man who had complete retention while wintering in Florida; a suprapubic cystotomy was done there and he returned to the city with the suprapubic drain in.

The day before operation the irrigation is done more frequently, and a thorough and prolonged irrigation is carried out the morning of the operation. Three hours before the operation he is given luminal, three grains, and half an hour before a quarter of a grain of morphine sulphate and 1/50 of a grain of atropine are given.

### THE OPERATION

The anæsthetic is most important. Ether presents the greatest hazard, because of the possibility of its inducing subsequent renal depression and acute pulmonary complications. Personally, I have not used ether for ten years. Gas anæsthesia is popular with many, but I have found the relaxation unsatisfactory and there is more trouble from hæmorrhage. Lundy has recently called attention to the deleterious effect of repeated cyanosis. Others have a preference for regional anæsthesia. My own preference has been for spinal anæsthesia, which I have used for more than fifteen years in 95 per cent of my prostatectomies. Until December, 1928, novocain (1.50 to 1.75 c.c. of a 10 per cent solution) was used, but since that time, spinocain, which I have found exceedingly satisfactory. With a specific gravity lower than that of the cerebrospinal fluid, the height of the anæsthesia is controlled, and with the use of ephedrin (grains 2) a fall in blood pressure is rarely seen. Pitkin says that the solution must be given with the patient lying down, but I prefer giving it with the patient sitting up, and as it only takes three to four seconds to place the patient in a recumbent position afterwards I have found no ill effect, and I think that the number of failures is less by this method. In the last six months more than 100 operations have been done under spinocain and in only 6 was it necessary to give either a little ethyl chloride or ether. I feel that for prostatectomies spinocain is now almost an ideal anæsthetic.

As soon as the spinocain is given the bladder is filled with saline and the catheter withdrawn. The vas on each side is localized with the fingers and a silk worm stitch is placed through the skin around it and tied to prevent epididymitis. With the patient's head lowered, an ample incision is made in the mid-line and the bladder exposed. With a trocar attached to the suction apparatus the saline is then withdrawn and the bladder emptied. The bladder is then widely opened and the prostate is inspected.

In some cases the dissection is done with the prostate in full view, but in the majority of cases I find it easier and more satisfactory to shell it out, while the assistant presses the prostate forward with his finger in the rectum. As soon as the prostate is removed the bed must be thoroughly inspected. All tags are cut off, any spurting vessels are ligated, and occasionally a running suture is placed around the edge of the prostatic pouch. With the assistant's finger still pressing upwards, a sponge on a holder is pressed downwards, or hot irrigations are used, to stop any oozing. I have been using a Pilcher bag in each case, but am beginning to feel that when you have the bleeding controlled perhaps the bag is not always necessary. In addition, a No. 30 French rubber catheter is placed in the bladder and a small piece of corrugated rubber drain in the space of Retzius. The bladder is then closed except for the catheter and the Pilcher tube, and the patient returned to his bed on a

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stretcher with his head still lowered. The foot of the bed should remain elevated for a couple of hours. After six to eight hours the Pilcher bag is deflated and next morning it is removed, as also the large rubber catheter. Each day the catheter is replaced by a smaller one and on the fifth day it is removed and a catheter placed in the penis. Three thousand c.c. of fluids, intravenously, interstitially, by the rectum and by the mouth, are given daily, and the bladder irrigations with acriflavine are continued. As soon as drainage ceases above, the catheter is withdrawn and left out during the day, to be replaced again at night. The shortest time of closing was 8 days, but the average time has been 20 days.

### MORTALITY

In the last one hundred cases there was a mortality of six. The causes of death were as follows.

*Shock.*—A man of 73 who died within twenty-four hours of operation. This was an early case and I would not operate upon such a one at the present time. Too much stress was laid upon normal blood chemistry findings, but the man never looked, ate, or slept well.

*Uræmia.*—A man of 81 years, who was progressing favourably for his operation, developed erysipelas. He was very ill for a month, had complete retention, and became intolerant to the catheter. A cystotomy was done, but he still suffered great pain, and was continually pulling the drainage tube out, and it was only with great difficulty that it could be put back. Though he did not come under the group of cases that were well, it seemed as if he had to be operated upon owing to the continual distress he was having. He died on the 9th day from suppression of urine.

*Embolus.*—Two patients died from embolus, one on the 14th and the other on the 24th day. They were both convalescing most satisfactorily. In fact, the operation wound in the latter case was healed and the man could have left the hospital a week previously. It seems that in prostatectomy deaths from embolus are more frequent than in any other condition. In the Mayo's report of 1,000 cases the mortality was 1 per cent; in my cases, 2 per cent. In gall-bladder cases, hysterectomies, and stomach cases it is only about one-sixth to one-quarter of 1 per cent.

*Sepsis.*—One man aged 73 died two and a half months after operation. He was making a satisfactory convalescence until about the third week, when his temperature went up; there was a suppurative epididymitis which was opened and drained, and a suppurative pyelitis which gradually brought about exhaustion and death.

*Cardio-vascular disease; chronic bronchitis.*—In one case death occurred fourteen days after the operation due to these conditions.

Since January, 1927, there have been 34 cases, with average age of 60, in whom a primary prostatectomy was performed, with a mortality of one-third of 1 per cent. The pre-operative treatment averaged 11½ days. The mortality rate was therefore satisfactory, and the pre-operative treatment was not prolonged.

The primary operation gives the best opportunity for accurate surgical intervention in the bladder, and consequently more accurate control of hæmorrhage.

There were two cases of epididymitis, or 6 per cent. The average time of voiding was 17 days, and for the closure of the wound 20 days.

### CONCLUSIONS

1. Patients must look well, eat well, feel well and sleep well before they are considered to be in condition for operation.

2. Primary prostatectomy in the great majority of cases is the operation of choice.

3. Spinal anæsthesia, preferably with spinocain, is the most satisfactory.

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The practical lesson to be learned from the newer knowledge of nutrition is the great importance to health, at all ages and especially in childhood, of giving a more prominent place, in our eating habits, and in our food budgets, to what McCollum has called "the protective foods," *i.e.*, to milk, fruit, and some of the vegetables; and that a "more tolerant" attitude toward sweets for children is not justified except in so far as the use of sugar and other sweets may be practically helpful in preserving the protective foods or facilitating their attractive preparation so that children may be induced to live more largely upon them.—*How to Live*, Jan. 1930.

# ECLAMPSIA*

By H. D. COWPER, M.B., M.R.C.S., L.R.C.P.,

*Welland, Ont.*

UNDER the term eclampsia are grouped all those cases of convulsions and coma occurring in pregnant women not due to extraneous causes, such as hysteria, epilepsy, tubercle of the brain, etc.

Not all cases of eclampsia present the same picture, and the term has been applied in common to cases presenting varying symptom groups. Some cases in their symptomatology and pathology resemble very closely the uræmic poisoning associated with deficient kidney function; others resemble acute yellow atrophy of the liver; while others, again, may present the picture of alkalosis.

Although it has not, so far as I am aware, been proved positively that an intoxication of the blood exists, the strong probability is that the condition is due to toxæmia of unknown origin, which produces necrosis of the liver, degenerative changes in the kidney, and also convulsions by direct toxic action on the anterior cerebral cortex and profound disturbances of metabolism. Whitridge Williams says, "With the exception of the nephritic type, neither pathologic study nor chemical analysis of the blood and urine gives any clue to the ultimate cause of eclampsia or any of the other forms of late toxæmia of pregnancy, and that in all probability it is due to some chemical substance which leads to profound disturbance of metabolism accompanied by certain organic lesions, but what it is or whether it originates primarily in the child, the placenta, or the mother is not known." The cause of the convulsions is also to a certain extent speculative. If the toxæmic theory were proved positively, the action of the toxins on the cortex of the forepart of the brain would be sufficient explanation, but it has been held that œdema of the brain, similar to the œdema existing in other organs, causes an increased intracranial pressure and as a consequence convulsions. This theory seems to me to be logical.

* Paper read at the meeting of the Ontario Medical Association, Hamilton, May, 1929.

## PATHOLOGY

The pathological changes found in eclampsia may be described as follows. In a large majority of the cases there is flattening and moderate œdema of the cerebral convolutions, sometimes with anæmia, sometimes with congestion. Small or large hæmorrhages, and areas of cerebral softening are also present.

Probably the most typical changes are found in the liver. These changes consist of albuminoid degeneration, with hæmorrhagic and anæmic necroses. These focal necroses occur near the small portal vessels, which are often thrombotic. In addition, there is fatty degeneration of the lobules which may be so marked as to resemble acute yellow atrophy (De Lee).

Almost always there are signs of disturbance in the kidneys which in some cases resemble the changes in acute nephritis. Cloudy swelling and fatty degeneration are the rule, and thrombosis in the glomeruli and smaller vessels is common. Further, all forms of subacute and chronic nephritis may be found.

Congestion and œdema of the lungs is frequently present, and there may be bronchopneumonia from aspiration of slime, blood, or vomitus.

## SYMPTOMS

The symptoms may be divided into those of the prodromal period and those of the actual eclamptic seizure. Of the latter little need be said, as every physician with any experience has seen these cases and the picture is indelibly impressed on his memory. Of the symptoms of impending eclampsia, however, much may be said, for it is on the prompt recognition of these prodromata that successful treatment of this horror of horrors is based. Early recognition and efficient treatment will many a time arrest the disease and save a mother from the worst catastrophe that can befall her.

Prodromal symptoms may be present from a

few hours to several weeks preceding the actual seizure. Headache, dizziness, a tendency to nervous excitation, somnolence, especially diurnal, and sleeplessness, cramps in the muscles, nausea, vomiting and, a most important symptom, pain in the epigastrium, spots before the eyes, dimness of vision, ringing in the ears, are all symptoms that demand a thorough exhaustive examination.

This examination will usually show some œdema of the feet and eyelids, or more or less generalized anasarea, with pasty skin and a coated tongue. There may be tenderness in the epigastrium. High pulse tension is usually present and the aortic second is usually accentuated. There is usually a diminished urinary output, with high specific gravity and hyaline casts and a diminished output of urea. Occasionally, the urinary findings are negative, but there are, nevertheless, œdema and high blood pressure. These cases are rare, and marked albuminuria with casts, together with reduction in the amount of urine, is almost constant.

After the onset of convulsions the symptoms of this condition are well known and very little need be said, except that labour usually commences if the convulsions are very severe and once commenced may be quite rapid. Occasionally, though rarely, the convulsions cease under treatment without interrupting the pregnancy, and the patient may go on to term and deliver a healthy living child. This happened recently in a case of my own, a young primipara who, after enjoying a particularly heavy Christmas dinner, complained of severe headache which lasted throughout the day, and late that night went into convulsions. The urine was highly albuminous; there was œdema; and the blood pressure was 165-80. Under an expectant, conservative treatment, her convulsions ceased, her blood pressure fell, and while she still retained her albuminuria she went on for four weeks to term and had a normal delivery with no untoward results. Since that time her albuminuria has entirely disappeared and she is apparently in perfect health.

Cessation of the convulsions, while it may occur and the child be still alive, is more often due to death of the fetus.

### PROGNOSIS

Statistics vary considerably when dealing with the mortality rate in eclampsia, Stroganoff giving 5.3 per cent and Buttres 45 per cent. I think, if a fair average were struck, we should be obliged to say that at least 20 per cent of eclamptics die and this figure is if anything conservative.

Eclampsia occurring in pregnancy is the worst, and the earlier it appears, the higher the mortality. Coming on during labour the mortality is less, while convulsions during the puerperium carry the lowest death rate.

The prognosis varies directly with the number of convulsions, and the greater the number the higher the mortality, although patients have died after two or three convulsions and have survived after twenty times that number. Anuria and intense albuminuria are both bad prognostic signs. The fetal mortality rate is also very high when the mother is the subject of eclampsia.

### TREATMENT

The treatment of eclampsia resolves itself into the treatment of the prodromal stage and the treatment after convulsions have set in, and of the two the first is by far the more important. All gravidæ should be looked upon as potential eclamptics and should be subjected to a complete detailed examination.

The past history is important and the occurrence of eclampsia in the mother, epilepsy or insanity in the family, acute infections, especially scarlet fever, or a history of "biliousness" or nephritis, should be viewed with a great deal of suspicion.

The blood pressure should be frequently taken and the urine examined at frequent intervals.

Upon the appearance of any of the prodromata, especially severe headaches, vomiting or pain in the epigastrium, when accompanied by generalized slight œdema, albuminuria, or an increasing blood pressure, the patient should be looked upon as an eclamptic and treated as such. She should be put to bed and saline purgatives freely administered. She should be given nothing but water for two days, and this in large quantities. If there is abatement of the symptoms, milk may be added

to the water and if still further improvement is noted in a few days, starches, and later vegetables and bread and butter may be given. Still later, a full vegetable diet may be allowed, with mild fruits and an occasional egg, but proteins other than this should be avoided. If, however, after two days of nothing but water there is no improvement, then the uterus should be emptied and the sooner the better.

The method of procedure is a matter of choice, depending on the conditions and the urgency of the case. In multiparæ when there is no urgency, simple rupture of the membranes will suffice, while in primiparæ, under the same conditions, passing a bougie into the uterus and packing the cervix tightly with gauze is the best method. In either case labour will usually commence in twelve to twenty-four hours. Here let me say that the most rigid asepsis and antisepsis must be observed because eclamptics or pre-eclamptics are notoriously prone to infection. As soon as the pains have effaced the cervix the membranes should be ruptured and dilatation aided by gentle manual manipulation.

Up to recently the use of pituitary extract was discouraged on account of its action in raising the blood pressure, but now since the separation of the uterine contracting hormone from the extract this hormone can be safely administered, as it has no effect on raising the blood pressure, while the contractions it causes are as strong if not stronger than in the case of the whole extract.

The treatment outlined above will take care of the vast majority of pre-eclamptics, but occasionally one will be confronted with a case in which the progression is so swift that some more rapid means of emptying the uterus is demanded. In these cases I think vaginal Cæcarean section should be done where possible, but in a primipara with a rigid cervix this is so difficult a procedure that abdominal Cæsarean section by the low method is quite justifiable. Here let me say that while in the pre-eclamptic, abdominal Cæsarean section may be quite advisable, I do not think it is ever justifiable after the onset of convulsions. Here the mortality rate is so high that it should never be employed. The addition of the shock accompanying this operation to a system already so poisoned as to show convulsions does not appeal to me as either logical or sane. In the pre-eclamptic be as radical as you choose in order to avert convulsions, but once they have set in be very careful not to add more shock than is necessary. Hence err on the side of conservatism.

When the case passes from a pre-eclamptic to a true eclamptic stage with convulsions the patient should be immediately transferred to hospital, if she is not already there, and placed in a quiet darkened room with a well trained nurse in constant attendance. The room should be well ventilated.

Every means should be adopted to prevent injury during the seizures. A large clothes pin, carefully protected, is a valuable aid in preventing biting of the tongue, and the elasticity of the prongs will take up the champing of the jaws. Artificial teeth should be removed, and the head turned on the side, to allow free drainage of mucus or vomitus, thus preventing aspiration of foreign material into the lung. No effort should be made to restrain the movements, but every care taken to prevent injury. For extreme jactitation morphia may be administered.

Chloral hydrate in twenty grain doses, with bromide of soda, forty grains, should be given by rectum in one hundred c.c. of saline, and repeated if needed. This is especially indicated if there is coma or delirium.

If the blood pressure is very high and the pulse bounding venesection seems to give good results.

Magnesium sulphate, 15 c.c. of a 25 per cent solution, may be given intramuscularly into the gluteal muscle, or it may be given in 20 c.c. doses, or as a 10 per cent solution intravenously. In either case the dose should be repeated frequently enough to control the convulsions, even every hour if necessary. If there are signs of respiratory failure, 5 c.c. of 10 per cent calcium chloride should be given intravenously. Magnesium sulphate exerts a relaxing and anæsthetic effect, but it also causes a marked reduction in the intracranial pressure and thus relieves the convulsions. In addition to the administration of magnesium sulphate intravenously, 60 c.c., of a concentrated solution should be given by mouth if the patient is conscious, or by a Levin tube through the nose if she is in coma.

Glucose 20 c.c. of a 50 per cent solution, should be given; it is better given in this way than by large doses of the 10 per cent solution, In the smaller dose of high concentration it does not increase the amount of the fluid in the tissues which is already excessive.

Frequently, labour commences with the onset of convulsions and should be allowed to proceed naturally if the condition of the patient does not demand more urgent interference. If this is the case dilatation should be aided by gentle manual manipulation, and the uterine contracting hormone of pituitary extract administered. So soon as the cervix is dilated and the head engaged forceps may be applied, or a version performed to expedite delivery.

If labour has not commenced the treatment should be medical first, and obstetrical only if necessary. Providing the convulsions can be controlled by magnesium sulphate and glucose, no attempt should be made to induce labour, but after the eclamptic attack is over labour may be induced if conditions warrant it.

If death of the fetus has taken place and the convulsions cease, then nothing is required, as nature will expel the fetus in due course. If, however, the convulsions cannot be controlled by the treatment outlined, and the condition is becoming urgent, something more drastic may be called for, and it may become necessary to perform a vaginal hysterotomy. In these cases the mortality rate is likely to be very high.

In conclusion, let me repeat that the guiding principle in the treatment of the pre-eclamptic stage should be radical, but in the convulsive stage decidedly conservative.

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## REPORT ON AN EPIDEMIC OF POLIOMYELITIS IN OTTAWA, 1929*

BY T. A. LOMER, M.D.,
*Medical Officer of Health of Ottawa, and*
W. T. SHIRREFF, M.D.,
*Superintendent of Strathcona Hospital,*
*Ottawa*

ON account of the prevalence of poliomyelitis in Manitoba in 1928, it was considered probable by the Ontario Department of Health that the Province of Ontario might be visited by the disease in 1929 and local health authorities were warned to be on the lookout for cases and to prepare lists of possible donors of convalescent serum.

### INCIDENCE

The first case of poliomyelitis reported in Ottawa was on July 28th, although subsequent investigation showed that there had been at least two cases in the vicinity during the previous week. All the earliest cases reported from the surrounding districts occurred to the west of Ottawa, and it would appear as though the disease had spread to this city from the west. Four cases were reported during the first week of the epidemic, seven the second week, and only one on the third, which gave rise to the hope that the epidemic was a small one and already on the decline. The fourth week, however, showed an increase to 16 cases, and it was evident that the epidemic was to be of serious proportions, as was subsequently borne out by the fact that for two months the weekly number of cases reported ranged from 11 to 25.

The incidence of the cases by weeks is shown in the subjoined chart.

In all 176 cases were reported which were considered definitely poliomyelitis. Of these 23 originated outside the city of Ottawa, but were brought into the city for treatment, some being residents of the city taken ill at summer resorts, and others being residents of neighbouring municipalities in Ontario and Quebec.

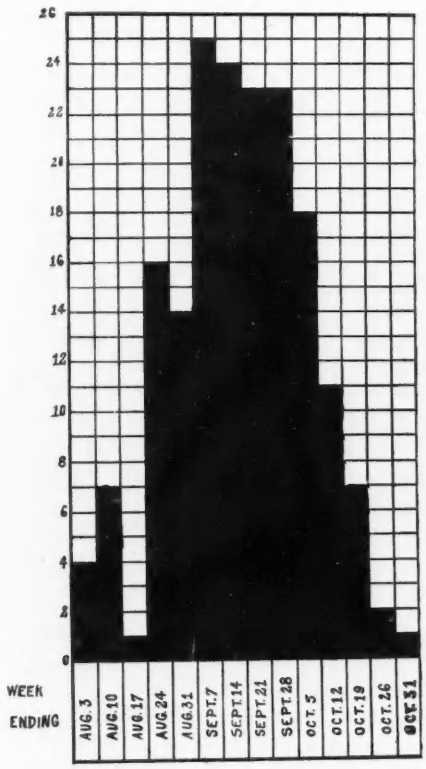
During the earlier part of the epidemic there was a noticeable concentration of cases in two districts of the city, one a medium class resi-

* Published concurrently and by arrangement with the *Canadian Public Health Journal.*

dential district near the centre, and the other a more wealthy residential district at the eastern edge. However, after a few weeks the disease had appeared all over the city with the exception of one district. Ottawa south was the last part of the city to be affected and no cases appeared in this large area during the first nine weeks of the epidemic.

The only section of Ottawa which showed no cases was the northwestern part, formerly known as Mechanicsville. This section is composed for

CHART I



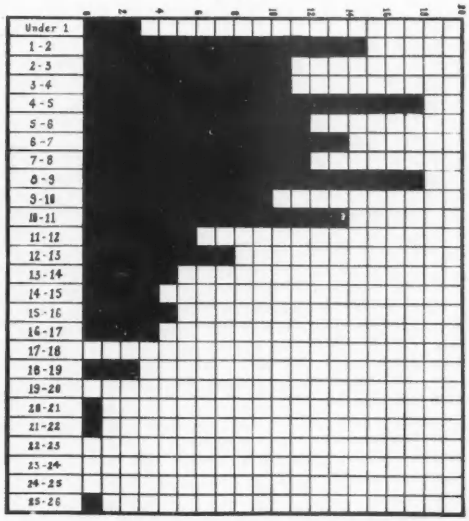

the most part of detached houses, chiefly of frame construction occupied by persons of small income and with large families. While the conditions here are by no means slum conditions it is probable that a combination of overcrowding and small financial means exists to a larger extent in this area than in other parts of the city.

Investigation of premises at which cases occurred did not reveal anything which would point to sanitary or social conditions, or the presence of flies or other insects, as being factors in the spread of the disease.

In only four instances were two cases reported from the same premises. In the first instance two out of three children of a family developed the disease three days apart. The next case was that of a maid of eighteen years who developed poliomyelitis six days after the only child in the house was affected. In another house the only two children became ill three days apart. The fourth instance is that of two children of 2½ and 4 years living in different apartments in an apartment house who developed the disease two days apart.

Climatic conditions during the course of the epidemic may be referred to only to mention that the weather locally was unusually fine, with more than the average of clear sunny weather lasting late into the fall and with a rainfall considerably below the average. The water level of

CHART II




the Ottawa River fell three and one-half feet below the average for the time of the year and many wells in the country districts surrounding the city were nearly or completely dry. The river level reached its lowest point on September 3rd and was still much below normal at the end of October.

The ages of the patients ranged from 7 months to 25 years, averaging 7.43 years with a maximum incidence between 4 and 5 and between 8 and 9 years.

A noteworthy feature is the comparative rarity of the disease during the first year of life, which emphasizes the undesirability of the term infantile paralysis.

The incidence by age is shown in Chart II.

Sixty per cent of all cases reported were males.

### CONTROL MEASURES

As the outbreak of poliomyelitis was not altogether unexpected the local health department had prepared a partial list of recovered cases of the disease who might be available as donors in case of necessity, and when the first cases were reported these donors were immediately called on and a limited supply of serum obtained. On August 10th, and again about a week later, a small supply was obtained from the Department of Health of Ontario in Toronto, but the demands from the rest of the province required most of their available supply. An additional amount of 350 c.c. was obtained from Winnipeg through the kind assistance of Dr. F. Cadham. The fact that during the third week of the outbreak only one case of poliomyelitis was reported misled us as to the amount of serum that was likely to be required and the large increase of cases the following week made it difficult to secure an adequate supply.

By advertising in the daily press the need for donors, we were able to secure a considerable number from the city and surrounding districts, but our chief source of supply was Crippled Children's Clinic. This clinic, which had been organized seven years ago through the efforts of the Rotary Club, numbered among its patients many whose disability was due to the effects of poliomyelitis. Through the energetic assistance of Mr. R. C. Cameron of the Rotary Club, who had access to the records of this clinic and who was personally acquainted with all the patients, we were quickly able to secure a large number of donors and throughout the epidemic these cases were called upon in groups and formed the mainstay of our serum supply. I wish to express my deep appreciation of the great assistance rendered by Mr. Cameron, and by Dr. J. Murray and Dr. G. Armstrong, the orthopædic specialists in charge of the clinic. It is largely due to their efforts that we were able not only to secure a supply of serum sufficient for the needs of the city but also to provide assistance to many cases in the surrounding districts.

In all fifty-nine donors were used and provided a total amount of 14,000 c.c. of blood. Their ages ranged from eight to thirty years, the mean age being between nineteen and twenty. The amount of blood withdrawn at a time ranged from 50 c.c. to 470 c.c., the average being about 200 c.c. Eight of the donors supplied blood twice. The length of time since the occurrence of poliomyelitis in the donors varied from two to twenty-three years, and averaged thirteen years. None of the cases occurring in this epidemic were used as donors.

The blood was paid for at the usual rate by the city and the money paid was refunded by the Ontario Department of Health who assumed the full cost of the supply of serum. The donors were taken in groups to the Ottawa Civic Hospital where the blood was withdrawn, and the serum was prepared in the Pathological Department of the Hospital by Dr. Thomas Little, whose assistance and co-operation were of the utmost value.

Dr. Little's description of the technique used in preparing the serum is given by him as follows:—

> A suitable vein was chosen at the bend of the elbow and the area was covered with tincture of iodine. A dental rubber tourniquet was applied. During the collection of the blood, the tourniquet was not removed and the donors were requested to open and close their hands at the rate of about fifteen times per minute to facilitate rapid withdrawal. A number 16 gauge, 1½ inch, needle was used with about 6 inches of rubber tubing attached to it.
>
> The blood was collected directly into sterile, 16 oz. ordinary, flat bottles, which were placed in the refrigerator in a slanting position of about 10 degrees and at a temperature of about 34 degrees F. for from eighteen to twenty-four hours. This allowed better shrinkage of the clot than would be obtained in an upright position.
>
> The serum was poured off into sterile containers. Five c.c. were cultured for possible contamination; about 2 c.c. were tested serologically for the Wassermann and Kahn reactions. The preservative used was tricresol 0.02 c.c. per 100 c.c. of serum.

After the second week of the epidemic it was apparent that, although a supply of convalescent serum was available, the cases were not being received at a sufficiently early stage for serum treatment to be of any value. It was evident, therefore, that both the medical profession and the public needed information as to the early signs and symptoms of the disease and required to be impressed with the importance of early diagnosis. With this end in view a circular was sent to every physician detailing the diagnostic features of the pre-paralytic stage of poliomyelitis, urging the importance of early treatment, and giving a list of consultants whose services could be called on without charge. A meeting of the Medical Society was called for the purpose of discussing the subject of poliomyelitis and a complete sym-

posium of this subject was given, particular attention being paid to the diagnosis in the pre-paralytic stage.

Consultants were appointed by the Board of Health from leading members of the profession in the city to act as diagnosticians in cases of suspected infantile paralysis. These consultants gave their services voluntarily.

To instruct the public, the daily press published articles giving the early symptoms of the disease and stressed the fact that it was curable if treated sufficiently early. Parents were advised to call in a physician if any suspicious symptoms were noted, and provision was made for free diagnosis and treatment for any who could not afford to pay. Throughout the epidemic the press published daily reports of the number of cases occurring and kept the public informed as to the progress of the epidemic.

As the epidemic was well established by the end of August the question was raised as to the advisability of postponing the opening of schools. It was the opinion of the Board of Health that nothing would be gained thereby unless at the same time all children were excluded from churches, Sunday Schools and places of entertainment, and also unless they could be prevented from congregating in playgrounds and on the streets. Moreover it was considered that the intelligent supervision of the school population by teachers and nurses might be a means of getting early medical attention to suspected cases. Many parents however decided to keep their children out of school and the attendance during September was from 15 to 20 per cent below normal, gradually increasing to 5 per cent below normal in late October. In the lower grades the attendance was particularly affected. Parents were not urged to send their children to school, and if they were summering in an uninfected locality were advised to remain there. It is noteworthy however that the disease was reported in at least five popular summer resorts, all situated in the Ottawa Valley to the west of the city. It is very doubtful if the closure of schools would show any beneficial result in controlling the incidence of poliomyelitis; at any rate, the epidemic reached its peak during the week that the schools opened and from that time gradually declined. Moreover, during the first few weeks of the school term the incidence of the disease among children of school age who had been kept out of school was proportionately as great as among those attending.

As there was ample accommodation and few other cases in the Strathcona Hospital, it was deemed advisable to treat all cases who so desired in this institution.

Eighty per cent, or 141 of the 178 definite cases, were admitted to the hospital and in addition 40 other suspected cases which were diagnosed as other conditions or whose symptoms and cell counts were not sufficiently characteristic to warrant a definite diagnosis of poliomyelitis. The patients were kept in hospital for three weeks and in no case did any cross infection occur and no return cases developed after discharge. None of the suspected cases developed poliomyelitis while in the hospital or after discharge, but it must be noted that nearly all these received 20 to 25 c.c. of serum on admission.

Those patients who were treated at home were quarantined in accordance with the Ontario Regulations. The patient was isolated, the house placarded, concurrent disinfection ordered, and terminal disinfection carried out. This last measure was in response to popular demand and to allay uneasiness rather than from any conviction as to its efficacy.

Children known to be exposed to the disease were excluded from school for ten days and kept under observation.

### REPORT OF POLIOMYELITIS CASES ADMITTED TO HOSPITAL

In all 181 suspected cases were brought to the hospital for diagnosis or treatment.

Fifteen of these cases had lumbar puncture done and, having a cell count of less than 10, and not sufficient specific symptoms to warrant a diagnosis of poliomyelitis, were sent home after receiving 20 c.c. of serum.

Twenty-five other cases that were admitted as suspected poliomyelitis were later diagnosed as other conditions or, on account of low cell counts (below 10) and lack of sufficiently diagnostic symptoms, were finally classed as doubtful cases and have been eliminated from the statistical report. All these also received serum at the time of admission when lumbar

The reference referred to on page 163 as appearing on page 231 is to be found on page 240.

XUM

puncture was done. In this group were found three cases of pneumonia, two of pyelitis, and one each of brain tumour, diphtheria, scarlet fever, acute rheumatic fever and meningococcus meningitis.

After eliminating all doubtful cases there remained 141 which were considered definitely poliomyelitis and which form the basis of this report. All these cases had a number of the cardinal symptoms, or a sufficiently high cell count, to warrant classing them definitely as positive cases.

Lumbar puncture was done in all but three cases except in those who had shown characteristic paralysis for some days before admission and where there could be no doubt as to the diagnosis. In most cases an anæsthetic was administered for the operation as it was found early in the epidemic that much more satisfactory results could be obtained thereby. Ether was used for children and a local anæsthetic for adults.

In eighteen cases no cell counts were made; fifteen of these were cases which were already paralysed on admission, and in three others the count was impossible owing to the presence of blood or for other reasons.

Five cases that had an initial cell count of less than 10 showed higher figures in subsequent counts, in one instance an increase from five to eighty after thirty-six hours.

The spinal fluids of 118 cases showed the following counts:—

| | |
|---|---|
| 10 to 25 cells | 38 cases |
| 25 to 50 cells | 29 cases |
| 50 to 100 cells | 31 cases |
| More than 100 cells | 25 cases |

Of the last group several counts were more than 200 and two more than 500 cells.

Convalescent poliomyelitis serum was administered to all cases in which paralysis had not been established for more than two days. Twenty-five c.c. was the usual dose, administered intramuscularly deep in the buttocks.

Early in the epidemic, the supply of serum being limited, only definite cases were given the injection, but later on when the supply was ample both definite and suspected cases were given serum at the time the lumbar puncture was done. In four cases a second dose of serum was given when after the initial drop in temperature the temperature rose again and the headache and rigidity persisted. No other treatment was given except that all patients were confined to bed for two weeks and any paralysed cases for the total time in hospital. Paralysed limbs were also immobilized.

The various subjective symptoms occurred in 141 cases in the proportions shown in the following table.

TABLE I

RELATIVE FREQUENCY OF SYMPTOMS IN 141 CASES

| *Symptom* | *Number* | *Percentage* |
|---|---|---|
| Fever | 124 | 88 |
| Headache | 92 | 65 |
| Rigidity of neck | 87 | 62 |
| Vomiting | 72 | 51 |
| Pain in back or limbs | 66 | 47 |
| Anorexia | 34 | 24 |
| Drowsiness | 30 | 21 |
| Apathy | 20 | 14 |
| Nausea without vomiting | 18 | 13 |
| Diarrhœa | 14 | 10 |
| Abdominal pain | 14 | 10 |
| Sore throat | 11 | 8 |
| Irritability | 11 | 8 |
| Dizziness | 6 | 4 |

*Fever* was present in all but seventeen cases, and nine of these were patients who were not seen until paralysis had set in, who had been ill six days or more. Eight only of those seen early had no temperature on admission. In very few cases was the fever more than 103°, the majority being from 100° to 102°

*Headache* was the next most common symptom. It was frequently described as severe and, when localized, was generally frontal. Headache together with fever and vomiting formed the three symptoms which were most prevalent early in the disease. Rigidity of the neck and pain in the back or limbs, which were considered more specific symptoms, did in some cases occur early, but in most cases were a later manifestation than fever, headache, and vomiting.

*Rigidity of the neck* occurred in 65 per cent of the cases and *pain* or *stiffness of the back or limbs* in 47 per cent, but in only 17 per cent of the total cases was neither symptom present, and of these ten were cases seen late and who were already paralysed. It might be of interest to call attention to the fact that the rigidity of the neck encountered in these cases is quite distinct from that seen in cerebrospinal or other specific meningitis. Seldom is there any retraction. The rigidity is elicited mostly when the head is bent forward past the middle line, and there is little on lateral movement.

*Abdominal pain* was present in 10 per cent of the cases and in two cases was so marked that a diagnosis of appendicitis was made.

*Tremor and sweating,* symptoms which had been reported as common in other epidemics, were noted in very few of our cases.

### CLINICAL RESULTS

| | *Number* | *Percentage* |
|---|---|---|
| Total cases treated | 141 | |
| Total cases recovered completely | 109 | 77.4 |
| Total cases recovered with paralysis | 29 | 20.5 |
| Number dying with paralysis | 2 | 1.4 |
| Number dying without paralysis | 1 | 0.7 |

Of the 31 showing terminal paralysis, 26 already had paralysis on admission, including two of the deaths, and our experience was that once paralysis was established the serum treatment had little effect on the result. This is not saying, nevertheless, what curative effect might result from massive doses of serum or repeated injections, as no experiments were made along that line.

Deducting the twenty-six cases that had paralysis on admission we have 115 cases. Of these:

| | *Percentage* |
|---|---|
| 109 recovered completely | 94.8 |
| 5 recovered with paralysis (2 of which were very slight) | 4.3 |
| 1 died without paralysis | 0.9 |

One of these cases which developed paralysis after receiving serum had, owing to a temporary shortage of serum, received only 10 c.c. on admission and developed paralysis within twenty-four hours thereafter.

As illustrating the importance of early diagnosis in preventing paralysis by means of early treatment with convalescent serum it is of interest to compare the terminal conditions of the cases received in hospital during the first four weeks of the epidemic with those admitted during the last nine weeks.

Early in the epidemic neither the medical profession nor the public was familiar with the early manifestations of poliomyelitis, but after the publicity given to this disease by the press and by means of circulars and medical society meetings, much earlier diagnosis was secured.

In the first four weeks of the epidemic, 23 cases were received in hospital. Of these 17 had terminal paralysis, (14 of these had paralysis on admission, 2 of whom died; 3 developed paralysis after receiving serum, all within twenty-four hours); 6 recovered without paralysis.

Of the subsequent 118 cases, 107 recovered completely; 8 had paralysis on admission, which in some cases was slightly improved on discharge; 2 developed paralysis after treatment, but so slight as to be difficult to diagnose; 1 died without paralysis.

Whether this bears out the contention that most epidemics of poliomyelitis are more severe at the beginning, or whether it were altogether due to the earlier diagnosis, cannot be answered, except to say the average time the total of 31 paralysed cases were ill before a diagnosis was made was four and one-half days. The average time the unparalysed cases were sick before diagnosis and treatment was one and one-half days.

The accompanying Charts show the extent of paralysis in two groups of cases. The severity

CHART III

| Case Number | Day of Illness on admission | Cell Count | PARALYSIS | | | | | | Condition on Discharge | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Right Arm | Left Arm | Right Leg | Left Leg | Face | Trunk | Cured | Improved | Unimproved | Died |
| 495 | 6 | – | 1 | 1 | 2 | 3 | | | | + | | |
| 496 | | – | | | 1 | | | | | | + | |
| 499 | 4 | – | | | | 1 | | | | | + | |
| 502 | 5 | – | | | | | 1 | | + | | | |
| 504 | 5 | – | 2 | | | | 1 | | | + | | |
| 505 | 4 | – | | 1 | | | | | | | + | |
| 510 | 4 | – | 2 | 2 | | | | | | + | | |
| 513 | 14 | 30 | 1 | 1 | 2 | 2 | | | | + | | |
| 514 | | | 3 | | | | | | | + | | |
| 530 | 6 | 250 | 2 | | 3 | 3 | | 3 | | + | | |
| 533 | | 80 | | | | 1 | | | | | + | |
| 535 | 3 | 60 | | | 1 | 1 | | | | | | + |
| 531 | 4 | 80 | | 1 | | 1 | | | | | + | |
| 539 | 4 | – | | | | 2 | | | | + | | |
| 545 | 5 | 25 | 3 | | | | | | | | + | |
| 554 | 4 | – | | | 3 | | | | | | + | |
| 561 | 4 | 31 | | | 2 | | | | | + | | |
| 589 | 4 | – | 3 | | | | | | | | + | |
| 601 | 1 | 88 | | 2 | | | 1 | | | | + | |
| 611 | 4 | – | | | 3 | | | | | | + | |
| 629 | 7 | 60 | | | | | 1 | | | | + | |
| 648 | 2 | 72 | | | 2 | | | | | | + | |
| 720 | 5 | – | 3 | | | | | | | + | | |
| 721 | 3 | 24 | | 1 | 1 | | | | | | + | |
| 725 | 10 | | | | | 1 | | | + | | | |
| 737 | 3 | 310 | | | 2 | | | | | | | + |

CASES ADMITTED WITH PARALYSIS

of the paralysis is indicated as— (1) slight; (2) moderate; and (3) severe. No attempt has been made to subdivide according to the part of the limb involved.

CHART IV

| Case Number | Day of Illness on Admission | Cell Count | Day Serum given | Amt. of Serum given | Day of Illness Paralysis appeared | PARALYSIS: Right Arm | Left Arm | Right Leg | Left Leg | Face | Improved | Unimproved | Died | REMARKS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 544 | 4 | 128 | 4 | 20 | 5 | | | 1 | 1 | | | + | | |
| 546 | 2 | 188 | 2 | | 3 | | | | | 1 | | + | | |
| 547 | 4 | 208 | 4 | 20 | 5 | | | 2 | 3 | | + | | | Mon. serum only at first Due to shortage |
| 626 | 6 | 120 | 6 | 20 | | | | | | | | | + | Died in 24 hrs. No Paralysis |
| 676 | 2 | 566 | 2 | 20 | ? | | | | 1 | | | | + | Paralysis very slight Noticed first |
| 718 | 2 | 58 | 2 | 20 | ? | | | | 1 | | | | + | when patients get out of bed |

CASES DEVELOPING PARALYSIS AFTER ADMISSION

## CONCLUSIONS

1. The treatment of poliomyelitis with convalescent serum administered in the pre-paralytic stage gave very good results.

2. The method of administration by intramuscular injection was simple and satisfactory.

3. The serum appeared to have little or no effect on those cases in which paralysis had begun.

4. The rapid fall of temperature and the improvement of symptoms after serum treatment have some significance as a therapeutic diagnostic test.

5. A limited supply of convalescent serum should be at all times available for use in sporadic cases or at the beginning of an epidemic.

6. Complete and up-to-date lists of the names and addresses of possible donors should be kept for use in epidemics.

7. Early in an epidemic the medical profession and the public should be reminded of the pre-paralytic symptoms of poliomyelitis and of the supreme importance of early diagnosis and facilities for diagnosis should be provided.

8. Definite information is desirable as to the relative therapeutic value of serum from treated and untreated cases.

9. Information is needed as to the possible efficacy of massive doses of serum given at the onset of paralysis.

## REPORT ON THE THREE FATAL CASES

### CASE 1

(No. 535) Female, age 7 years. Previous history irrelevant. Illness began August 17th with vomiting and difficulty in swallowing followed by fever, gradually became worse with high fever, difficulty in speaking clearly, choking spells, and at times twitching of muscles of arms and neck. Hypersensitive to noise.

When seen August 19th at 6 p.m. she had high fever and marked languor. Speech indistinct, but no delirium. Very apprehensive, especially when asked to drink. Marked dysphagia and suggestion of spasm of throat muscles simulating hydrophobia. Slight photophobia, some stiffness of neck muscles, occasional twitching of muscle bundles in arms and neck. Kernig's sign, doubtful. Reflexes normal.

At 8 p.m. neck stiffer. No retraction. No paralysis except of speech. Sent to hospital the same night. On admission was unconscious. Temperature 102.° Cell count 60.

She died in coma August 20th, eight hours after admission.

No autopsy.

### CASE 2

(No. 537) Female, age 4½ years, admitted August 19th, who had been sick for three days with vomiting, headache, stiffness of neck and later pain in right arm. She was taken to the Civic Hospital where a lumbar puncture was done. Cell count 310.

Transferred to Strathcona Hospital same day. On arrival she showed marked weakness of right leg, pain in arms, back and legs. She was given 20 c.c. of convalescent serum. Twelve hours later she developed twitching of muscles, which soon subsided. Twenty-four hours after admission developed convulsions and died in ten minutes. No paralysis of respiratory muscles. No autopsy.

### CASE 3

(No. 626) Male child, age 2½ years, admitted 4 p.m. September 12th. This patient took ill on September 7th with headache, stiffness of right leg and some fever. On September 8th the fever persisted and he was nauseated. On September 9th, the patient seemed better but later the fever returned and the stiffness of the neck and headache became more severe. He was brought to the hospital on the sixth day of illness. Lumbar puncture showed a cell count of 120. The temperature on admission was 105° and patient appeared extremely ill. There was no paralysis on admission.

Twenty c.c. of serum given but the patient gradually became worse developing rigidity of the limbs fifteen hours after admission and he died three hours later.

This patient showed no definite paralysis at any time, and did not develop convulsions.

No autopsy performed.

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RETENTION OF URINE CAUSED BY FÆCAL IMPACTION.—I was called out to see a boy, aged 3½ years, who had been having severe colicky pains in the abdomen all night and that day. As he had not vomited the mother had not sent for me before. On examination the cause of pain was obvious, the bladder being distended up to the umbilicus. I found a well-marked phimosis and took the child straight into hospital. A circumcision was performed, and an attempt made to catheterize the bladder. No instrument could be passed, and, suspecting a calculus, a finger was introduced into the rectum, which was found to be filled with hard fæces. After a large quantity of this material had been removed, a catheter passed freely into the bladder. I have heard of this occurring in a female child, but never in a male.—J. Myles Mitchell, M.B., B.Ch., *Brit. M. J.* **1**: 1198, Dec. 28, 1929.

# Case Reports

## A CASE OF INFECTIOUS MONONUCLEOSIS

BY L. C. MONTGOMERY, M.D.,

*Montreal*

Miss E., aet. 21 years, was admitted to the Montreal General Hospital on May 31, 1929.

*Complaints.*—Swelling on both sides of the neck; slight sore throat; feeling miserable.

*Family history.*—Negative.

*Personal history.*—She had always lived in Ontario and Quebec, and had had the ordinary children's diseases; scarlet fever at 11 years (stated to have been complicated with pneumonia, pleurisy, and endocarditis), when she was in bed for five months; influenza in 1918; an infected finger, August, 1927; "la grippe" in December, 1928; acute sinusitis in January, 1929. She had had sore throats at intervals since January, 1929.

*Present illness.*—The patient had not been in her usual good health since January, 1929. There had been anorexia and slight general malaise for four weeks prior to admission, and she had had rather frequent sore throats. She had also lost weight. On May 31, 1929, she suddenly became quite ill, feverish, and felt that her neck was painful and swollen. Her throat was only slightly sore. She was admitted to the ward on the following day.

*Physical condition.*—The patient was well nourished, but rather pale looking. The head was held stiffly as if she was suffering from mild torticollis. Pulse, 72; blood pressure, 94/64; respirations 22; temperature 99.2° F. The teeth were negative, except that the margin of the gum hung over the right lower posterior molar and bled on slight pressure. The tonsils were not hypertrophied, but were red, and exudate could be expressed. There was a generalized tenderness and enlargement of the cervical, submaxillary, axillary, and inguinal glands. These varied in size from that of a large pin head to that of a Brazil nut, and were discrete. The chest was negative. There was no increased dullness under the manubrium sterni.

The abdomen was soft, but presented slight generalized tenderness. The spleen was palpable just below the left costal margin, tender, and enlarged to percussion. The liver was not palpable. No petechiæ were present on the body or limbs.

*Urine analysis.*—Sp. gr. 1020; a trace of albumin; no glucose; microscopically negative.

*Blood examination.*—(On June 1, 1929), red blood cells, 4,560,000 per c.mm.; white blood cells, 15,000; platelets, 110,000; hgb. 89 per cent (Sahli); bleeding time—3 minutes; polymorphonuclears 23 per cent, lymphocytes 71 per cent, mononuclears 6 per cent, reticulocytes 2 per cent. The lymphocytes showed a nucleus with a peculiar lobulated appearance (bilobed or Rieder type of nucleus).

*Impression.*—Most likely an infection of the mononucleosis type, but acute lymphatic leukæmia was to be considered.

Six days after admission the physical examination was unchanged, and, if anything, the patient was brighter, so it was felt that acute lymphatic leukæmia could be definitely excluded. There had been no hæmorrhagic phenomena.

The striking points were the sudden onset of fever, malaise, stiff neck, and the generalized glandular and splenic enlargement.

By the ninth day after admission the glands were becoming definitely reduced in size, but the spleen was still palpable.

Her general improvement continued, and she was ready for discharge from hospital on July 5, 1929, thirty-five days after admission. During this time her temperature had gradually subsided, but there was still a slight daily elevation. The highest temperature recorded was on the 9th day of her illness at 101.6° F. The glands in the neck were "shotty," and the spleen was still palpable.

All the special examinations, including a blood Wasserman test, were essentially negative, except for a basal metabolic rate of plus 17, and evidence of an old pleuritis at the right base. The Von Pirquet test was negative. Smears and cultures from the tonsils showed no spirochætes or fusiform bacilli.

On discharge (July 4, 1929) the blood picture

was as follows: red blood cells, 4,490,000; white blood cells, 4,500; platelets 115,000; hgb. 80 per cent (Sahli); bleeding time, 2 minutes; coagulation time, 9.5 minutes; polymorphonuclears 46 per cent, lymphocytes 39 per cent, mononuclears 4 per cent, eosinophiles 4 per cent.

In September, 1929, the patient had a tonsillectomy done in Rochester, New York, and had quite a severe post-operative bleeding. Just prior to the operation her blood examination was as follows: red blood cells 4,550,000; white blood cells, 4.576; hgb. 82 per cent (Sahli); "A diminished platelet count" (the actual numbers not given in report); polymorphonuclears 58 per cent, lymphocytes 39 per cent mononuclears 2 per cent, eosinophiles 1 per cent.

The patient returned to her work on November 1, 1929, with a moderately good colour; pulse 68; tonsil beds clean. A few small glands were palpable in the cervical regions, but the other superficial glands were not palpable. The spleen was not palpable, but there was tenderness under the left costal margin on deep palpation. Splenic dullness was still slightly increased; liver not enlarged. A blood examination on November 7, 1929, showed: white blood corpuscles 5,400; platelets 207, 000; bleeding time, 3½ minutes; polymorphonuclears 57 per cent, lymphocytes 43 per cent. No immature cells were noted.

At the end of five months there is still a relative increase of lymphocytes, although the physical examination is essentially negative.

This persistent relative increase in lymphocytes is the characteristic finding in infectious mononucleosis.[1]

REFERENCE

1. DOWNEY, H., AND MCKINLAY, C. A., *Arch. Int. Med.* **32:** 82, July 1923.

## A CASE OF RAT-BITE FEVER

BY J. STEWART MURRAY, M.D.,

*River John, N.S.*

George H., aged 17; white, Canadian. The family and personal history were negative.

This boy, of more than average intelligence, made a practice of amusing himself by catching rats in the barn with the aid of his dog. On July 13, 1929, he cornered one in a box, and in an attempt to kill it he was bitten just above the nail on the left index finger. The superficial scratch, 8 mm. long, he treated with Tr. Iodi., and it healed promptly without apparent trouble.

On July 18th, five days later, he felt a soreness in the left axilla, with chilly sensations and malaise the same evening. The pain in the arm and axilla prevented him from sleeping most of the night, and on the morning of the 19th, when he came to my office, the malaise was more marked. The boy was pale and appeared quite ill; temperature, 99°; pulse, 80.

The site of the bite on the finger was negative, except that it was slightly tender on deep pressure, but there was a very marked lymphangitis extending from the base of the index finger to the axilla. The streaks were together about 3 cm. wide, red, hot, slightly swollen and tender, especially so at the elbow and axilla, but there were no palpable glands. Other systems were negative.

I applied a hot wet dressing of bichloride of mercury (1-2000) to the whole arm, with directions to change it every two hours.

July 20th. When I saw the boy at his home in the morning, I found the temperature 104,° the pulse 100. The pain in the arm was better, but the limb was still slightly stiff. The lymphangitis was gone. He complained of pain in his back and legs, and headache, and appeared to be very ill. A leucocytosis of 28,200 was present. The wet dressing was discontinued.

I sent a specimen of blood to Dr. Ralph P. Smith of Halifax, for bacteriological examination. He reported as follows: "Direct blood films from patient. No spirochæta morsus muris detected. Result of guinea pigs intraperitoneal inoculations. Blood films after fifty hours, negative. The two guinea pigs are seemingly quite well. Blood cultures. One of them gave a pure growth of staphylococcus albus while the other gave a profuse growth of B. subtilis. (Usually a contamination)."

July 21st. A.M. His temperature was 104°; pulse, 106. There was a leucocytosis of 18,400. The boy was restless, complained of headache, and there was a blotchy erythematous measles-like rash over the whole body. The left epitrochlear gland was palpable and about the size of a bean; the axillary glands, negative. The urine was negative, except for a slight

trace of albumin. In the afternoon the temperature fell to 100° and the rash was fading.

I gave him 0.45 gm. novarsenobenzol intravenously, with some resulting reaction controlled with 5 mm. of adrenalin. Later, he was nauseated and vomited.

July 22nd. A.M. His temperature was 99°; pulse, 86; leucocytes 25,800. He was feeling much better; the rash had faded still more. The epitrochlear gland was the same and there were several small glands palpable in the left posterior cervical triangle. In the afternoon the temperature was 104.6°; no rash.

July 23rd. A.M. Temperature 99°; pulse 76; white blood cell 8,800. The rash had returned, though it was not so brilliant or generalized as at first, but it was very marked over both feet and the posterior surface of the elbows, where there were a few pustules. It was also present on the face and buttocks and in the afternoon it became more generalized and brilliant. There was complaint of pain in the dorsal surface of the right foot during the night. The rash did not recur again. Temperature, of a gradually declining intermittent type, continued until August 12th.

On July 26th I gave a second dose of 0.6 gm. novarsenobenzol; on August 6th a third dose of 0.6 gm.; and on August 14th a fourth and final dose of 0.6 gm., to make sure that the last traces of infection had been overcome.

August 27th. White blood cells, 9,600; hæmoglobin 85 per cent. The epitrochlear gland was still enlarged. The appetite was good, and the boy apparently was normal, with his strength rapidly returning.

As this disease is rare in Canada it seemed worth while reporting this case. It is regretted that the diagnosis could not be confirmed by the bacteriological examination. Unfortunately, the related lymph glands were never large enough to permit of puncture with a needle and aspiration of fluid for animal inoculation, or of excision and injection of an emulsion.

Inoculation of blood and direct smears for the *Spirochæta morsus muris* often fail, as they did in this case. Blood culture proved sterile for ordinary pyococci causative of an ordinary septicæmia. The clinical course of the disease so closely followed that of rat-bite fever and the response to novarsenobenzol, the accepted treatment for this condition, was so prompt that an error in diagnosis could hardly be possible.

The incubation period of five days was a little shorter in this case than usual, that is from ten to twenty-two days. The usual characteristic symptoms were well marked, namely, lymphangitis and adenitis of the regional lymphatic system in the neighbourhood of the bite (which may have been completely healed by the time of the onset of symptoms); leucocytosis and paroxysms of fever of the intermittent type, preceding the eruption of a blotchy erythematous rash resembling that of measles; headache; generalized pains in the muscles and joints.

The organism responsible for this disease is more of a spirillum than a true spirochæte, and was discovered by Futaki, Takaki, Taniguchi, and Osumi in Japan, in 1915, where the disease is quite frequently met with. The organism is found in the skin, lymph glands and the blood.

I wish to extend to Dr. Smith my cordial thanks for his interest and valuable assistance in this case.

## SEVERE HÆMORRHAGE FROM A RUPTURED LUTEIN HÆMATOMA*

BY H. W. JOHNSTON, F.R.C.S.,

*Demonstrator in Obstetrics and Gynæcology, Toronto General Hospital*
*Toronto*

Severe hæmorrhage in the peritoneal cavity from a ruptured tubal gestation is not uncommon; that from a ruptured lutein hæmatoma is rare.

Such a condition, according to the literature, was recognized as early as 1851 by Nélaton. Edward Moore,[1] in 1922, reviewing the literature to date, reported 13 cases, one of which was reported by Dr. Primrose, of Toronto, in 1912. Kaboth[2] and Hesselberg,[3] in 1923, reported cases. In 1924 cases were reported by Eick[4] and Schickele[5]. In 1929, also, 3 cases were reported by Levi[6] of St. Mary's Hospital, London, England. In English and American literature little mention is made of this condition.

If we consider the development and life

* Read before the Section of Obstetrics and Gynæcology, Academy of Medicine, Toronto, October 22, 1929.

history of the corpus luteum it is clear that there are three stages and in each stage profuse hæmorrhage may occur.

*The first stage.*—The time of ovulation. The ovum is expelled and the granulosa cells take on lutein characters. At this time it is not uncommon for serious hæmorrhage to occur from the ripe Graafian follicle, several cases of which have been reported.

*The second stage.*—Active growth of the corpus luteum takes place between the time of ovulation (usually the 14th day) and the 19th day of the cycle, taking the first day of the menstrual period to be the beginning of the cycle. Here we get the large lutein cells packed tightly together, forming the typical yellow coloured convolution, and the smaller theca interna cells scattered at the periphery and entering the septa of the lutein convolution.

*Third stage.*—The corpus luteum persists in its mature state and is responsible for producing the changes in the uterus preparatory to the embedding of the fertilized ovum, and the richly lipoid body which is found in the old luteal hæmatoma just as the next menstrual period commences.

There is really a *fourth stage*—the gradual replacement of the corpus luteum by hyaline tissue forming the corpus albicans, it taking in all nine months for the lutein cells to disappear entirely.

It was at the end of the second stage, or the beginning of the third stage, of the life history of the corpus luteum that the serious hæmorrhage occurred in the case I am about to report.

Mrs. P., housewife, aged 39, VI—gr., 11—para, was admitted March 29, 1929, complaining of severe right-sided lower abdominal pain and of feeling faint. The first day of her last menstrual period, which was normal in its duration and flow, had been March 9, 1929. Her appendix had been previously removed.

On examination, her temperature was 98.4°; pulse 140 and thready. A catheter specimen of urine was negative for red blood cells, white blood cells and casts. The patient was waxy in appearance and her abdomen was tender in the right lower quadrant and rigid over the entire lower part, more so on the right side than on the left. No free fluid could be made out. Vaginal examination under an anæsthetic showed no urethral or cervical discharge. The uterus was forward and normal. The fornices appeared clear.

Posterior colpotomy disclosed much blood. On opening the abdomen nearly a pint of blood escaped, and the blood was found to be coming from the right ovary, which was removed. The right tube, uterus, left tube and ovary, appeared to be normal, there being no adhesions or any sign of a previous inflammatory process. The patient made an uninterrupted recovery.

*Pathological report.*—"The ovary is normal in size. At one pole is a small clot protruding from a ruptured corpus luteum. Microscopic: the ovary contains many large corpora albicantia and a well developed luteal hæmatoma which has ruptured. Sections showed no evidence of chronic ovaritis."

### REMARKS

The causes given for such a condition are:—

1. Injury.—There was no history of trauma as the patient was awakened from her sleep with the pain.

2. Previous infection.—Section of the ovary showed no inflammatory change.

3. An exceedingly vascular organ.—This is a possible cause, as the rupture occurred just before the next period was due.

4. Rupture through the weakened spot caused by extrusion of the Graafian follicle. This may be the case here, as the rupture occurred in that part of the hæmatoma where the ovarian tissue was thinnest.

I desire to express my thanks to Dr. P. L. Irvine, of Toronto, to whom I am indebted for the case.

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## AN OVERLOOKED CASE OF SCURVY

BY J. C. DIAMOND, M.D.,

*Fort William, Ont.*

I was called to see a little girl of four years of age. The mother gave a history that the child had been in perfect health until six months before, when she became "cranky" on account of a toothache and was given a push by the mother. The child fell and could not use her legs. She was taken to several doctors

but treatment did not help. She next went to a chiropractor who "set her spine" and "replaced her hips," but still the child refused to walk.

When I was called to see her, she was lying on her back, with her knees acutely flexed, and the muscles of the thighs, legs, and buttocks badly wasted. The child screamed with pain whenever one attempted to touch her legs. Everything else was normal, except that her teeth had all been extracted. On asking why they were extracted, her mother said that they were very bad and her gums were swollen, and a doctor had told her that the child was suffering from rheumatism caused by these bad teeth. The teeth were extracted but she was not any better.

I made a diagnosis of scurvy and placed the child on orange juice and on the third day she was on her legs without pain. Massage and heat were applied to the legs, and the child was walking after two weeks' time.

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## AN "ANCIENT" CASE OF EMPYEMA OF THE FRONTAL SINUS

BY J. PRICE BROWN, M.B.,

*Toronto*

A young lady consulted me about twenty years ago. She was bright and had a good complexion, but she had frontal sinus disease. The whole of the right side of the head was swollen and red. I examined the nose internally and could find no discharge of pus coming from the sinus. The question was, what to do. I arrived at the conclusion that there was perhaps an abscess forming there, and that it ought to be drained. One of the leading Chicago specialists at that time was Dr. Ingles, who advocated using a silver tube in frontal sinus cases, passing it through the sinus into the nose. I had the idea of the tube in mind and I thought if the sinus were opened and a silver tube passed into the nose the patient might recover. So I had one made before I operated. To give you an idea of what the condition was, the surface over the sinus was much swollen and inflamed. After chiselling into the bone in a line with the eyebrow, a surgeon standing by said. "That is a case of sarcoma." I said it could not be. There was considerable pus in the cavity and some induration. I curetted it out, drilled into the nose, and passed the tube down through the sinus into the nasal cavity, leaving it in position. Then I thoroughly sterilized the cavity and sewed up the outside completely. The patient recovered and there was scarcely perceptible deformity, the eyebrow covering the scar in large measure. After the healing of the wound and the removal of the tube through the nose there was no return whatever of the sinus disease.

At that time I did not know much about frontal sinus disease and its connection with osteomyelitis, but I knew there was infection there, and that was the result.

[The above Case Report formed part of a discussion, to which Dr. Price Brown contributed, on Dr. Skillern's paper at the meeting of the American Laryngological, Rhinological, and Otological Society held in San Francisco early in July last year. It has been forwarded to the *Journal*, together with a very interesting letter, by Dr. Brown.

Dr. J. Price Brown, of Toronto, is well known to the older generation of medical men, at least, as a specialist in oto-laryngology. His text-book on "Diseases of the Nose and Throat", published thirty years ago, was a recognized authority on the subject, and was on the recommended list of books at Toronto University and the New York Polyclinic. He also entered the realm of fiction, bringing out during the next five years four novels dealing with Canadian life—Hickory of the Lakes; How Hartman won; In the Van; and The Macs of '37.

Dr. Brown has been retired from active work for fifteen years, during ten of which, unfortunately, he has been blind. Despite his handicap and his advanced years he was able to attend the meeting above referred to, where he was received with acclamation, and took part in the discussion of several of the papers.—ED.]

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INFLAMMABLE THROAT LOZENGES.—Dr. J. Pereira Gray writes: A policeman on cycle patrol duty felt a slight sore throat. He bought some chlorate of potash lozenges and put them in his trousers pocket, which contained a box of safety matches. After cycling for a few minutes he thought he heard a slight explosion; a minute later he saw flames issuing, which burnt a large hole in his pants and trousers, caught his coat and waistcoat, and scorched his skin in several places. He managed to extinguish the flames, and, on investigating their cause, he noticed that the live heads of his matches were now dead and his lozenges had disappeared. This episode shows that if potassium chlorate lozenges and safety matches are carried about they should not be placed in the same pocket. . . . The danger is not so much from the match heads as from the red phosphorus on the box, as anyone can prove by gently rubbing a chlorate of potassium lozenge along the side of an empty safety matchbox.—*Brit. M. J.*, Nov. 23, 1929.

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# Retrospect

## SOME NOTES ON OUR PRESENT KNOWLEDGE AND IGNORANCE OF THYROID FUNCTION*

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The title of this paper was chosen deliberately, to permit me to select those aspects of thyroid chemistry which appeal to me, and not to commit me to pose improperly as in any way an authority on thyroid function; further, to emphasize the importance of what has still to be discovered in dealing with discoveries already made. Every important discovery dazzles us and we are usually blinded for a while to the surrounding darkness which, after all, its bright light seldom more than feebly penetrates.

The history of thyroid investigation well illustrates the perfectly logical development of discoveries which, looking forwards from the midst of conflicting statements and incomplete data, we cannot prophesy, but which, looking backwards, appear to have been the inevitable culmination of the various researches that preceded them.

One of the most outstanding discoveries yet made about the thyroid gland is a therapeutic one—that administration of thyroid gland to a myxœdematous patient will restore that patient to a normal condition. It followed logically upon the association of atrophied thyroids with the cretinoid state and myxœdema and the beneficial results of grafting thyroid tissue in cases of myxœdema.

Dr. George R. Murray, at that time Lecturer in Bacteriology and Comparative Pathology in the University of Durham (later, Professor of Systematic Medicine in the Victoria University of Manchester), in 1891 at first injected, and subsequently fed, "thyroid juice" (glycerol extract of fresh sheep thyroid) to a woman of 46 who presented the typical picture of advanced myxœdema. Three months later[1] he reported "The swelling has gradually diminished, and has practically disappeared from the backs of the hands . . . The lips are much smaller . . . The swelling of the upper eyelids has diminished . . . The swelling beneath the eyes and of the cheeks has also much diminished . . . the face has greatly improved in appearance and has much more expression as many of the natural wrinkles especially about the forehead have returned. The speech has become more rapid and fluent . . . the mind has become more active and the memory improved. She is more active in all her movements . . . She has menstruated normally during the past six weeks." Dr. Murray made a final report on this case in 1920[2]. She enjoyed excellent health until early in 1919, when "she developed œdema of the legs and died in May of that year at the age of 74 from cardiac failure. This patient was thus enabled, by the regular and continued use of thyroid extract, to live in good health for over 28 years after she had reached an advanced stage of myxœdema. During this period she consumed over nine pints of liquid thyroid extract or its equivalent, prepared from the thyroid glands of more than 870 sheep."

The extraordinary improvement produced in a second case of Dr. Murray's by a few months of this treatment is shown pictorially in the *British Medical Journal* of August 27th, 1892[3].

An even more spectacular case was reported finally in 1924 by Dr. Hugh M. Raven[4], whose father had published the earlier reports in 1894 and 1897[5].

Mrs. S. developed myxœdema in 1870, at the age of 41; no treatment was instituted for over 20 years. At the end of this period she was bedridden, bald, and imbecile. Treatment with thyroid extract was commenced in 1893, and within 15 months she was practically normal, even to well-marked growth of hair. She continued a normal existence until 1924, living "to a ripe old age—happy, healthy, and mentally active," and dying finally of bronchitis. The photographs of this case are unusually striking.

The beneficial results of thyroid treatment in myxœdema were rapidly confirmed by many investigators in Great Britain, Germany, and elsewhere. Undoubtedly, this discovery was one of the chief factors leading to that intensified chemical study of the gland which commenced in 1893 and led to Baumann's discovery of the presence of iodine in 1895, and which is still continuing.

I would select as the outstanding chemical (and pharmacological) discoveries concerned with thyroid function some such list as the following:

1. Baumann's discovery that the thyroid tissue contains iodine.
2. Oswald's isolation of iodothyroglobulin.
3. Kendall's isolation of thyroxine from thyroid tissue.
4. Harington's determination of the nature of thyroxine.
5. Marine and Kimball's prophylactic use of iodine compounds for the prevention of goitre in children.
6. von Fellenberg's development of a method of estimating iodine so delicate that we now have really accurate knowledge of its distribution throughout the mineral, plant, and animal kingdoms.
7. The association of thyroid activity with 40 per cent of the normal heat production of the body.
8. Plummer and Boothby's use of Lugol's solution in lowering the hyper-metabolism associated with Graves' disease.

I propose to comment on each of these, briefly.

The first Chair in Biochemistry was created in 1883 in the University of Strassburg. Emil Baumann was its recently appointed occupant in 1895. His discovery of iodine in thyroid tissue was one of those examples of the importance of making accidental discoveries. He investi-

*A paper read to the Biochemical Section of the Dominion Chemical Convention at Toronto, May 30th, 1929.

gated the substance produced by boiling thyroid tissue with sulphuric acid. This, which he called (later on) "iodothyrin" we now believe to be merely a mixture of compounds and of no particular importance. But he fused it with alkali and tried the effect of nitric acid on the fused product. To his surprise he observed that iodine was liberated. His main claim to fame rests upon his accurate observation of this accidental discovery[6]. Although this discovery was made in 1895 it was not until many years later that one could assert definitely that iodine is an invariable constituent of thyroid tissue. In 1911, when I first became interested in thyroid problems, many investigators were still claiming that some thyroids contained no iodine. Such statements were due to the inaccurate methods of estimation then employed, and our more precise knowledge we owe to the elaboration of more accurate procedures, such as those of Hunter[7] and of Kendall[8].

Oswald, of Zurich, made the first really accurate investigation of thyroid proteins. His method and his results were published in 1899[9] and have during the succeeding 30 years scarcely been bettered or altered. He showed that treatment of fresh thyroid tissue with normal saline, and subsequent half saturation of the saline extract with ammonium sulphate and dialysis of the resulting precipitate gave a white globulin containing most of the iodine of the gland, and which he named *iodothyroglobulin*. Recently, Ingvaldsen showed[10] that this is not a true globulin, since, when freshly prepared, it is soluble in distilled water. Purification by alcohol precipitation denatures it so that it is no longer soluble. If someone could discover a method of purification which would enable us to obtain this compound in pure and soluble condition such a process would be of considerable value.

Though conclusive proof is wanting, I think we can consider that this thyroid "globulin" is the storage form of iodine in the functioning thyroid. It is true that Hektoen, Carlson, and Schulhof[11] have shown by precipitin methods that it is present in the merest trace in the lymph leaving the thyroid gland, and it is true also that other internal secretions such as insulin and secretin have been shown to have molecules of a complexity at least that of proteoses. But the general consensus at present is that the internal secretion of the thyroid is not complex in character, and leaves the thyroid by its veins.

The many attempts to obtain a crystalline iodine derivative from the thyroid were failures until E. C. Kendall succeeded in isolating thyroxine in crystalline form on December 25th, 1914.[12] He needed several further years of work to be able to prepare it at will and isolate it in reasonable quantities.[13] Misled by a slight analytical error, due apparently to its volatility during fusion for iodine analysis, he regarded it as a tryptophane derivative. Efforts to obtain it synthetically failed.

In 1926-28 Harington, by a brilliant series of researches, completely clarified our knowledge of the constitution of thyroxine[14], established it as a derivative of di-iodo-tyrosine—the only other iodized amino-acid found in nature—synthetized it with Barger[15], and finally has done what in all probability Ingvaldsen was only prevented by illness from doing in 1925[10], has isolated its precursor di-iodo-tyrosine from thyroid tissue[16].

Numerous researches by many investigators in the United States, in Canada, in Great Britain, and Germany, have established beyond doubt that thyroxine shows in every qualitative respect the full activity of the thyroid gland's secretion. Quantitatively, its action is less.

Having considered the important facts that we know concerning the chemistry of the internal secretion of the thyroid we can now glance at the still very important and large gaps in our knowledge of that secretion.

First, how is thyroxine elaborated? We may reasonably assume by the doubling up of two molecules of diiodotyrosine. And we may presume the existence of a specific enzyme. But these are only assumptions and presumptions. Proof is entirely wanting.

How is diiodotyrosine itself formed? Its formation is not specific to thyroid tissue. Sponges and corals form it and build its radical into spongin and gorgonin. Its radical is formed in proteins treated with iodine. Probably in such a slightly alkaline medium as that of blood hydrogen peroxide and an iodide would liberate sufficient iodine to give an iodo-protein. Ingvaldsen's work in my laboratory suggests that all iodoproteins (except iodothyroglobulin) contain their iodine entirely or almost entirely in diiodotyrosine radicals. It is true that Oswald and others have succeeded in isolating but small amounts of diiodotyrosine from such iodo-proteins, but Ingvaldsen obtained evidence that the yield can only be small by the methods so far employed.

What is the physiological action of thyroxine minus its iodine, *i.e.*, of desiodothyroxine, which Harington now proposes to call thyronine? And what will be the actions of the corresponding bromine and other derivatives when these are prepared?

Van Dyke's investigations[17] on the distribution of iodine within the gland suggested that it is present chiefly in the acini, but to some extent in the secreting cells lining these acini. These presumably form the active compound and it is then stored in the acini. Is it built up into thyroglobulin for storage purposes and then split off as required? This would appear to be probable but there is no proof of it.

Here are many interesting problems awaiting solution.

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I have previously stated that the quantitative action of thyroxine is less than that of thyroid containing the same amount of iodine. I shall now refer to the experimental bases for that statement. Kendall in his monograph states "The three possible methods (for determining the value of any particular thyroid preparation) are: the influence of the thyroid on the basal metabolic rate of patients with hypothyroidism or on thyroidectomized animals; the effect on the growth of small animals; and the effect on the resistance of the white mouse to acetonitrile"[18].

The first method is not easily applicable without a number of myxœdematous patients being available for test, so that for biological standardization of thyroid material we have to utilize either the acetonitrile test of Reid Hunt[19] or the effect on growth and the production of organ hypertrophy in young white rats[20].

Reid Hunt, in 1904, investigating the pharmacological action of acetonitrile, fed thyroid to rats and mice with the idea of increasing their oxidative catabolism, and so causing a more rapid liberation of hydrocyanic acid, and therefore a greater toxic effect from the acetonitrile. The toxicity to rats was increased by this thyroid feeding, but thyroid-fed mice displayed an increased resistance to this poison. Seeking for a test to serve as a biological assay for thyroid Hunt found that the increased resistance conferred on mice by thyroid feeding is proportional to the iodine content of the thyroid fed. Testing thyroxine by this procedure he has found that whether it be fed or injected a dose containing a certain amount of iodine only confers about two-thirds the degree of protection given by thyroid containing the same amount of iodine[21].

With the assistance of Mr. John Carmichael I started some experiments in 1919 to ascertain whether or not thyroid feeding decreased or increased growth-rate in the young rat, since the evidence at that time was decidedly conflicting. We were able to prove definitely that the growth-rate is decreased, and at the same time confirmed the observations of various investigators that many of the body organs hypertrophied under the treatment. We were gradually able to place our experiments on a quantitative basis and to evolve a system of biological assay using the double effects just stated, of which Kendall says: "It is interesting to note that by this method results were secured which compared favourably with the results obtained by the use of Hunt's acetonitrile method; and, although larger amounts of material are required, the influence on the growth of the white rat undoubtedly gives an accurate index of the physiological activity of the material."

Our method is more time-consuming and less elegant than Hunt's, but it forms a useful adjunct to his. Testing thyroxine by this method we have found that for equal iodine dosage it is somewhat less active than desiccated thyroid[22]. This statement applies equally to Squibb's thyroxin (prepared by Kendall's method), to Burroughs and Wellcome's thyroxine (prepared by Harington's method) and to their synthetic thyroxine (prepared by the method of Harington and Barger[23].

Before discussing the cause of this discrepancy I wish to refer—in an aside—to the curious difference exhibited by rats and mice to the acetonitrile test, and also to the rat test. Robertson has recently published the results of feeding thyroid to mice[24]. The body organs hypertrophy as usual, but the growth-rate is *accelerated*, not decreased. He suggests that the discrepancy may be due to one of three causes, a specific difference in the reactions of rats and mice to thyroid, (as shown also by the acetonitrile test), or the difference in technique of dosage employed, or a difference in the physiological equivalence of the dosage employed. I believe on theoretical grounds that the latter two suggestions can be disregarded. He and I are both at work on this peculiar discrepancy and the matter should shortly be resolved. In any case it would seem that an extended comparative series of pharmacological studies with these two closely related species might give even further results both curious in nature and of theoretical importance.

We must next consider why thyroxine does not quantitatively exhibit the full activity of thyroid tissue. One possible explanation is that the thyroxine that we have all been testing is optically inactive, while the thyroxine secreted by the gland is almost certainly active—and by analogy with adrenine, twice as active, physiologically, as the racemic compound. Harington has already helped to solve this point. He has resolved the compound into its optically active constituents and finds them *both* active[25]. Using the increase of oxygen consumption by rats as a test he finds that lævo-thyroxine is about three times more active than its isomer, from which it should follow that it should be 50 per cent more active than the racemic mixture. This fact might just account for the discrepancy between thyroxine and thyroid if *all* the iodine of the thyroid were in the form of thyroxine radicals, but such is far from being the case. The most that so far has been isolated as thyroxine is 15 per cent. We used to consider that the part of an alkaline hydrolysate of thyroid which is precipitated by acid, 30 to 40 per cent, represented the thyroxine fraction. Kendall now thinks that this is not the case[26]. In his most recent paper he has advanced evidence and theories that are somewhat confusing[27], and which, until confirmed, I think we should be somewhat cautious in accepting. But in any case we may state with certainty that thyroxine does not represent *more* than the acid-insoluble portion of the alkaline hydrolysate of thyroid tissue, and therefore represents less than half of the iodine of the thyroid, so that even lævo-thyroxine does not represent more than half the physiological activity of thyroid based on iodine content.

I have always thought of the possibility that the actual active secretion may be somewhat more complex than thyroxine itself. Kendall, on the other hand, seems to consider that thyroxine is the secretion, and is rendered more active by some chemical change to it in the cells in which it functions. He suggests such possibilities as the presence of an additional hydroxyl group tacked on by the cell. But this should be equally possible when thyroxine itself is fed. I think that all hypotheses will have to wait upon further experimental evidence.

Marine's work on iodine prophylaxis, and von Fellenberg's work on iodine distribution are intimately connected. It is somewhat easier to consider the latter first. von Fellenberg's method consists of a refinement of Bourcet's, essentially fusion, solution, treatment with nitrite and acid, and extraction of the liberated iodine with chloroform[28]. But the delicacy of his refinement permits the detection of such small amounts of iodine that he has had to coin a new unit, the microgram, one-thousandth of a milligram, to which he has assigned the Greek letter *gamma*[29]. Lunde, of Norway, his pupil, uses his method; McClendon of Minnesota and Hercus and others in New Zealand use similar ones.

McClendon commenced to stress the relationship between goitre and low values of iodine in food and water in 1922[30]. In 1923, von Fellenberg published the first part of one of the most complete and exhaustive researces that has yet appeared on the distribution of any element[29]. This work was undertaken for the Swiss Goitre Commission, and in many ways surprisingly confirms the much earlier work of his compatriot Chatin[32].

We are especially concerned with those results bearing upon the distribution of goitre, and I would draw your attention to the following striking facts.

McClendon's maps of goitre-incidence in recruits in the United States and of relative high

and low values in iodine content of the drinking water throughout the United States are remarkably similar[33].

von Fellenberg's data for iodine distribution in soil, food, and urine, contrasted with the incidence of goitre in certain Swiss districts and one Italian coastal district, show definite inverse proportionality. Some of these data are shown in Table I (it must of course be remembered that plants growing in coastal districts benefit to some extent by iodine in the air—sea-spray).

Hercus, Benson and Carter[36] have also published a striking curve showing the reciprocal relationship between the percentage of iodine in the soil in different New Zealand districts and the incidence of goitre amongst children.

These and many similar results permit us to state that in goitrous districts the food and drink of man is relatively low in iodine, due primarily to a deficiency in soil iodine affecting both vegetables and through them animals and affecting drinking water. A conclusion associating goitre with this deficiency cannot be avoided. One point still unsettled is whether or not this is the sole cause of ordinary simple goitre.

TABLE I.

INVERSE PROPORTIONALITY OF IODINE DISTRIBUTION AND INCIDENCE OF GOITRE

| *District* | *Goitre* | *Urine-I 24 hrs.* | *Rock-I per kg.* | *Earth-I per kg.* | *Salad-I per kg.* | *Milk-I per kg.* | *Eggs-I per kg.* |
|---|---|---|---|---|---|---|---|
| | % | γ | γ | γ | γ | γ | γ |
| Kaisten | 62 | 19 | 400 | 1400 | 50 | 73 | 147 |
| Hunzenschwil | 56 | 17 | 500 | 600 | 44 | 85 | 89 |
| Hornussen | 12 | – | 800 | 5000 | – | – | – |
| Effingen | 1 | 64 | 7000 | 12000 | 34 | 276 | 215 |
| Forte dei Marini | 0 | 112 | 360 | 6000 | – | – | – |

Lunde's data for certain Norwegian districts are in agreement[34]. Certain of these are shown in Table II.

TABLE II.

INVERSE PROPORTIONALITY OF URINE-IODINE AND INCIDENCE OF GOITRE

| *District* | *Goitre* | *Urine-I (24 hrs.)* |
|---|---|---|
| | % | γ |
| Hostvedt | 60 | 40 |
| Ljöterud | 54 | 29 |
| Verp | 36 | 87 |
| Ruud | 30 | 61 |
| Vik i Sogn | 0 | 173 |

The New Zealand data are also in general agreement. For example, Hercus and Roberts measured the actual iodine intake per person per day of 20 people in a goitrous and 20 people in a non-goitrous district for two separate fortnights[35]. The average results are shown in Table III.

TABLE III.

INVERSE PROPORTIONALITY OF IODINE-INTAKE AND INCIDENCE OF GOITRE

| *District* | *Goitrous Children* | *Mean I-intake per person per day* |
|---|---|---|
| | % | γ |
| Taranaki | 7 | 35 |
| Canterbury | 62 | 20 |

McCarrison has brought forward evidence that simple goitre can be induced by some bacterial or similar agency carried by supposedly goitre-producing waters, and can be cured by the administration of intestinal antiseptics[37]. This view is not generally accepted. Yet, he has recently recorded[38] that a change of drinking water from an iodine-containing and bacteriologically impure source to a bacteriologically pure water containing practically no iodine caused the disappearance of goitre from the Sanawar girls' school (in Northern India) where it was previously prevalent.

Keith has suggested the possibility that water may contain iodine in unassimilable form[39]. He noted that in the Pemberton Valley, B.C., where, previous to the prophylactic use of iodine the incidence of goitre was more than 80 per cent., the drinking water was very turbid, with a heavy sediment, and yet contained 103 parts of iodine per million, while Vancouver, with a clear drinking water completely devoid of iodine, has a goitre incidence of only 8 per cent. Generally speaking, where goitre is prevalent in British Columbia the drinking water is turbid and murky.

We may reasonably ask what is the effect of iodine-deficiency on the aboriginal inhabitant. Has he through long generations produced a race capable of thriving on a smaller iodine intake than the rest of the world require for normal existence? Hamilton and McCrae[40] report that Indians in Southern Manitoba are free from

goitre, although this is distinctly a goitrous district. The Alberta Tuberculosis Survey of 1924 found an incidence of 9.4 per cent of goitre amongst the Indians of Alberta. Keith[41] found that the Indians of Pemberton Valley, B.C. and their animals were the only living inhabitants of the Valley who did not develop goitre, while their surroundings were certainly more insanitary than those of the whites living there. But these Indians ate large quantities of salmon, and all marine fishes are excellent sources of iodine. On the other hand Carmalt Jones[42] reports that endemic goitre has been prevalent (known as "tenga") in some districts in New Zealand as far back as Maori tradition goes, and to-day in the Urewera district in the North Island, where the most primitive existing Maoris are now found, 18 per cent of 300 persons were found to have goitre.

The assumption that goitre was due to deficiency of iodine led to Marine and Kimball's work. But the ingestion of iodine as a preventive of goitre was recommended by Prévost of Geneva as long ago as 1849, and tried in Austria in 1855 and in Italy in 1859, and failure of the treatment was then due to over-dosage. Back through the dark ages such iodine containing mixtures as burnt sponge and seaweed were empirically employed. But the first systematic attempt to combat goitre on the large scale was commenced by Marine and Kimball in the schools of Akron, Ohio, in 1916. In these schools 56 per cent of the girls from the 5th to 12th grades inclusive were found to have goitre. To those who volunteered, and whose parents permitted, 3 gm. of sodium iodide were given twice a year in drinking water over a 10-day school period for 4 years. Of 2,190 pupils so treated only 5 developed thyroid enlargement, while of 2,305 not so treated 495 developed an enlargement. Of 1,282 with thyroid enlargement at first examination 773 thyroids decreased in size during the treatment, while of 1,048 with thyroid enlargement and untreated only 145 decreased in size[43].

Almost at once, similar large-scale experiments were tried elsewhere. Klinger obtained markedly curative effects in Zurich, using iodostearin tablets. Then the Swiss Commission advocated the use of iodized salt. Very good results were obtained. Thus Eggenberger reports that in Herisau before this prophylaxis 50 per cent of the babies were born with a definite palpable and visible enlargement of the thyroid, while from 1925 to 1927 inclusive he had not seen a single congenital goitre in 260 babies examined[44]. Good results have been obtained wherever this prophylactic measure has been tested, in Italy, in New Zealand, in Derbyshire, everywhere. The iodine has been given chiefly as sodium iodide tablets in chocolate, and as iodized salt.

These results not only indicate that goitre can and should be controlled, but also confirm the theory that lack of iodine in the diet is the main predisposing cause of the development of simple goitre.

There are two important problems on which we require more data, one theoretical, but the other of considerable practical importance. Precisely why does lack of iodine lead to, first, a hyperphysiological, and then, a pathological, hypertrophy of the thyroid? How much iodine should be administered to prevent development of goitre?

There seems to be considerable agreement amongst members of the medical profession that in certain types of goitre administration of iodine leads to severe symptoms of hyperthyroidism—the so-called toxic adenoma[45]. Hence some, at any rate, amongst them seem adverse to general iodine prophylaxis amongst the whole population. Believing in the doctrine of the greatest good for the greatest number I believe we should be willing to expose a small percentage of the population to some danger if we can, and there is strong evidence that we can, abolish goitre from the coming generation by compulsory iodine administration. If this be sound doctrine, then there is no better method of supplying iodine than by compulsory iodization of table salt. Nevertheless, if we do this, in view of the danger, even though it be a slight, and possibly imaginary danger[46], to some small part of the present goitrous population it is necessary and only just that we should limit the amount of iodine added to the necessary minimum. What is that minimum? The New Zealand authorities, basing their figure largely on the difference between the iodine ingested in the diet in a goitrous and a non-goitrous district in New Zealand, use only *4 parts of potassium iodide per million of sodium chloride*. In Switzerland very similar proportions are now used. These are very different from the *one part of potassium iodide per ten thousand of sodium chloride* at present used in Canada. Is the smaller amount enough? I believe that an authoritative committee should be appointed in Canada to investigate this matter and to report to whomever can take action.

Basal metabolic rate determinations are essentially measurements of heat production of the organism under resting conditions. Many thousands of determinations have shown conclusively that, with the exception of certain conditions such as leukæmia and certain cases of anæmia, the basal metabolic rate, with normal body-temperature, is only abnormal when thyroid function is abnormal, and that then it can range from — 40 to + 100 per cent of normal, *i.e.*, the heat production can vary from 60 to 200 per cent of the normal production. This range of variation depends upon the degree of functioning of the thyroid gland, from total lack of function (corresponding to the 60 per cent of normal heat production) to marked hyperfunction. Under normal conditions, therefore, the internal secretion of the thyroid is responsible for 40 per cent of the heat production of the body, and since heat production is a summation of the heat produced by all the oxidations of the body it is

obvious that to this extent the thyroid secretion controls these oxidations. How does it do this? What actually does the thyroid secretion do? We may well believe that thyroxine catalyses oxidative processes, but proof of this, and ideas as to how it is done, are still lacking.

In 1922 and succeeding years Plummer and Boothby[47], of the Mayo Clinic, demonstrated that astonishing results could be obtained by the administration of that solution of iodine in potassium iodide which we call Lugol's solution to cases of Graves' disease. The high basal metabolic rate falls, the pulse falls, there is increased well-being, there may be gain in weight, and, most important as a result, operation in this condition is rendered comparatively safe. The treatment does not replace operation. If the treatment be prolonged the basal rate again rises. Various theories as to the cause of the beneficial effect have been advanced. None of the present theories can be regarded as entirely satisfactory.

It is very doubtful if iodides produce any definite effect; certainly none is produced comparable to that following administration of Lugol's solution. Iodine in hydriodic acid solution is not quite so effective as Lugol's solution[48]. Recently some rather astonishing observations have been made bearing upon this phenomenon.

Apparently from the work of Harvey, of the Rowett Research Institute of Aberdeen, Dr. I. M. Rabinowitch, of the Montreal General Hospital, got the idea that a combination of vitamins and iodized fatty acid might produce the same effects as Lugol's solution. At his suggestion the firm of Ayerst, McKenna, and Harrison prepared a concentrate of vitamins A and D and iodized jecoleic acid. Dr. Rabinowitch and Dr. E. H. Mason, (the latter of the Royal Victoria Hospital of Montreal) both obtained good results with this preparation. The former has recently published his data[49]. Through his courtesy and that of the firm mentioned I was enabled to test the preparation, although I strongly disbelieved in the likelihood of good results, since these would disagree with the theory of the action of Lugol's solution that appealed to me. Dr. Gilbert Adamson and I were able, through the co-operation of the clinicians of the Winnipeg General Hospital, to test the preparation on a dozen patients. The results are definite. This mixture of iodized fatty acid and vitamins does everything that is done by the very powerful solution of iodine in potassium iodide in the pre-operative treatment of Graves' disease; no less, and no more, except that in no case so far recorded has it caused that gastro-intestinal disturbance sometimes provoked by Lugol's solution. The vitamins alone, and the iodized fatty acid alone, appear to be ineffective[50]. Recently, Dr. Roy Fraser and I have extended this work by substituting sodium iodide for the iodized fatty acid. We have obtained precisely similar results[51].

Why does a mixture of vitamins A and D and sodium iodide behave like the most active pharmacological form of iodine we possess? What have vitamins to do with the proper assimilation of iodine by the thyroid? Are both the vitamins necessary, and, if not, which of the two is the effective compound? These are more interesting problems for future solution.*

I believe that with a considerable use of controlled imagination, along with the accumulation of more facts, most of the problems that have been mentioned will be solved within the next dozen years. But without application of trained imaginations we shall not get very far.

I wish to acknowledge my indebtedness to Kendall's valuable monograph[52] in the preparation of this paper. There is little missing from the monograph and nothing superfluous, nor are there many of his conclusions that seem unacceptable.

* Very recently I have obtained some evidence that D is the essential vitamin (Sept. 1929).

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# Clinical and Laboratory Notes

## MECONIUM IN VERTEX PRESENTATION

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*Montreal*

The escape of meconium with the amniotic fluid in vertex presentation has a definite clinical significance. It signifies that the fetus at some time during the pregnancy or labour has been asphyxiated to a degree to cause suffocation hyperperistalsis and suffocation relaxation of the sphincter. Experimental work carried out by myself has proved quite conclusively, I think, that there is an interval of from fifteen to twenty minutes between the evacuation of meconium by the fetus and the appearance of that same meconium at the mother's vulva. If this is a logical and true conclusion, it puts a new interpretation upon the escape of meconium-stained amniotic fluid.

It occurred to the writer that as the consistence of meconium is generally of a tarry nature, it must take a considerable time to dissolve and diffuse itself in the amniotic fluid. This was put to the proof. A quantity of freshly evacuated meconium was taken and placed in a goodly quantity of fresh amniotic fluid. By stirring the fluid at half minute intervals currents were set up, which, in the writer's opinion, might simulate those produced by fetal movements and by uterine action. The amniotic fluid was kept at body temperature. By repeating this many times, with new stocks of meconium and amniotic fluid from different sources, it was found that it took from fifteen to twenty minutes for the amniotic fluid to become so coloured by the meconium as to be unmistakably diagnosed. If this be true, and it is amply corroborated by clinical evidence, then we must put a new interpretation upon escaping meconium-stained amniotic fluid. We have but to recall how frequently every obstetrician has hastened the delivery owing to escaping meconium, only to find the child vigorous and healthy, and showing not the slightest sign of asphyxia. Yet asphyxia there must have been owing to the presence of the evacuated meconium. The only interpretation admissible is that asphyxia is a short-lived condition, ending fatally or not, according as there is a sustained or fleeting causation respectively. Although fetal distress causes the evacuation of meconium, by the time the meconium has diffused itself by the solvent effect of the amniotic fluid and by fetal and uterine movements, and has flowed from the fundus to the vulva with the escaping currents, the child has either succumbed or the threat has passed off. If the fetus should be in distress, and meconium should be escaping at the same time, the natural assumption would be that the fetal distress has repeated itself and the escaping meconium was evacuated in the earlier suffocation.

Escaping meconium should not be taken as a sign of fetal distress. It should be merely an evidence of how commonly fetal distress occurs and how frequently the cause of the asphyxia is removed before fatal results ensue. This knowledge should make us put the proper interpretation upon the escape of meconium, namely, that it means only that the child has suffered, but should not be taken as a sign that the child is still in distress. Escaping meconium should teach us to determine, firstly, that the child is still alive, and, secondly, to realize that fetal cardiac action, judged by its rapidity or its slowness, by its arrhythmia or its variations in intensity, is the only reliable evidence that fetal distress is actually taking place.

## TREATMENT OF FRACTURES OF THE OS CALCIS BY ARTHRODESIS OF THE SUBASTRAGALAR JOINT

BY J. A. NUTTER, M.D.

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Fractures of the os calcis are followed as a rule by marked disability. Cotton and Wilson[1] have stated that there is permanent disability in more than 50 per cent of cases. Magnuson[2] estimates the permanent disability as ranging from 30 per cent to 75 per cent in practically each foot. The treatment of other fractures shows good and ever better results, but fractures of the os calcis have as heretofore continued to lead all other fractures of the bones of the leg in the disability they produce.

The victim is usually a man about 42 years of age. He falls from a height on his heels. The inner side of his foot being elastic gives away, driving the foot outwards. The os calcis breaks, as is natural, in front and back of the main articular facet, on which the astragalus sits carrying the body weight, and the heel portion is pushed out and upward, flattening the arch of the foot. The sides of the os calcis balloon outward against both the external and internal malleolus, and the bone is found to be well to the outer side of where it should be immediately under the astragalus to support the body weight. In addition, the important joint between the astragalus and os calcis is ruined beyond repair, while often the plantar surface of the bone becomes so roughened by fragmentation that it cannot sustain the body weight without pain.

Efforts to restore the os calcis to form and function are usually utter failures. The powerful tendo Achillis resists any attempt to pull the heel down. It is very difficult, even with a mallet and sand bag, to narrow the bone to normal and drive it back under the astragalus. As for the joint with the astragalus above, this is hopelessly damaged. A permanently painful flat foot is the usual result. It may be remembered that attention was drawn to the prominence of the os calcis laterally, where the bone widened out below the external malleolus and rubbed against it. At the time this was thought to be the source of much disability, and operations were devised to hammer it back or chisel it away. The results were disappointing.

Now we are being told that the disability is largely in the damaged astragalo-calcaneo joint. This joint, it is pointed out, is badly injured and yet has to sustain the weight of the body. Also the foot is flat as a result of the accident, thus causing muscular and ligamentous strain. It would seem logical to cut down on this joint, push the os calcis back into its normal position just under the astragalus, and fix it there by an ankylosing operation. The assumption is that the joint between it and the astragalus is now of no practical value and is only a source of pain. The disability from this ankylosis, if the foot is in good position, is practically negligible. Plaster fixation is for eight weeks, with weight bearing on the plaster after six. Dr. P. D. Wilson, of Boston, the orthopædic surgeon who, with Cochrane, now of Edinburgh, wrote one of the best books on fractures and dislocations, is a warm advocate of the operative method mentioned above. His recent article on the subject is both interesting and convincing[3]. He has treated 26 patients by operation, with results so encouraging that he is now extending the operation to fresh fractures. He quotes Van Stockum[4] as first publishing the procedure. Recently it has also been recommended by Conn *et al*[5,6,7]. It would seem that this most baffling surgical problem is now in process of solution.

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## GRAM-STAIN: A FURTHER MODIFICATION

Air-dry the film and fix with the least amount of heat necessary. Flood with dye for five minutes. Previously mix 30 drops of a 1 per cent aqueous solution of crystal violet or methyl violet 6B with 8 drops of a 5 per cent solution of sodium bicarbonate. Allow the mixture to remain for five minutes or more. Flush with iodine solution for two minutes. (2 grm. iodine dissolved in 10 c.c. normal sodium hydroxide solution and 90 c.c. water added.) Drain without blotting, but do not allow film to dry. Add a mixture of equal parts of acetone and alcohol drop by drop until the drippings are colourless (10 seconds or less). Air-dry the slide. Counterstain for 20 seconds with 0.1 per cent aqueous solution of basic fuschin. Wash off excess stain by short exposure to tap water, and air-dry. If slide is not clear immersion in xylol is recommended.—Kopeloff, N., and Cohen, P., *Stain Technol.* **3:** 64, 1929.

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# Editorial

## THE PROPHYLACTIC VALUE OF BACILLUS CALMETTE-GUÉRIN

PROPHYLACTIC vaccination with B.C.G. has been an outstanding subject for debate during the past two years. While the conclusions of Professors Calmette and Guérin have gained wide acceptance on the continent of Europe, it must not be forgotten that they have been violently opposed elsewhere, notably by Professor Lignieres, a veterinary expert of Buenos Aires, and in English-speaking countries they are still *sub judice*. The importance of the matter naturally led to much experimentation in different countries, in the hope of clearing up some of the points that were in need of review. Of special interest to us here in Canada is the fact that much important work has been done by Prof. Allan Rankin[1], of the University of Alberta, and his collaborators, by Dr. E. A. Watson[2] and his associates of the Research Laboratory of the Federal Department of Agriculture, at Hull, Que., by Dr. J. A. Baudouin[3], of the University of Montreal; in England by Dr. A. Stanley Griffith[4], under the auspices of the Medical Research Council, and by Dr. S. A. Petroff[5] and others in the United States. In addition to the destructive criticism of some, at least, of the laboratory investigators, the statements of Calmette and Guérin have been reviewed with damaging effect, from the statistical side, by others elsewhere, notably Greenwood[6] in England, and Rosenberg[7] in Germany.

In October, 1928, a special conference, attended by some of the most renowned bacteriologists, veterinaries, and clinicians in the world, was held at the Pasteur Institute, Paris, under the auspices of the Section of Hygiene of the League of Nations, where Professor Calmette[8] presented a detailed report on his method of vaccination, based on the results obtained up to that date in various countries of the world, a report in which he reiterated his faith in the harmlessness and efficacy of B.C.G. vaccine.

So far as Canada is concerned the only clinical work with B.C.G. has been conducted by Dr. Baudouin and his associates, of the Department of Hygiene of the University of Montreal. From June 23rd to June 30th, 1928, the number of infants vaccinated with B.C.G. in Montreal was 615. In no case was there the least reaction or illness referable to the vaccine. Dr. Baudouin concludes that the procedure is harmless, and that the micro-organism is not virulent and does not become so. Unfortunately, this opinion was not controlled by post-mortem examinations, which were lacking altogether.

Lignieres in his attack on Calmette and Guérin's work referred to the researches of Dr. Watson and his collaborators (*loc. cit.*) which were begun in 1924, shortly after the publication of Calmette's first paper. The Canadian workers directed their attention first to the pathogenicity of the micro-organism composing B.C.G. Out of 134 guinea pigs inoculated with B.C.G. 30 were found, on death or slaughter, to have tuberculous lesions, and 12 had generalized caseating tuberculosis. These investigators considered that they could eliminate the possibility of spontaneous or naturally acquired tuberculosis in their animals, and were also confident that there had been no contamination of their cultures. They concluded, after three and a half years' work, that the strain of tubercle bacillus composing B.C.G. had not been entirely deprived of virulence; that this virulence was a latent property of the organism, requiring some unusual stimulus and especially time to awaken it into activity; and that it was

1. RANKIN, A., Rep. Nat. Res. Coun. (Canada) p. 21, 1927-28; also. *Ann. d. l'Inst. Pasteur* **43:** 878, July, 1929.
2. WATSON, MCINTOSH, AND KONST, Rep. Veter. Dir. Gen., Dept. of Agricult., Can., p. 40, 1929.
3. BAUDOUIN, J. A. *L'Union Médicale du Canada*, **58:** 274, 329, 1929.
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5. PETROFF, S. A. *et al.* Forty-fourth Ann. Med. Rep. Trudeau Sanatorium, 1928.
6. GREENWOOD, M. *Brit. M. J.* **1:** 793, May 12, 1928.
7. ROSENBERG, S. *Wien. klin. Wchnschr.* **41:** June 7, 1928.
8. CALMETTE, A., *Ann. Inst. Pasteur*, Paris, **42:** 1, Supp., December, 1928.

capable in guinea pigs, after a long period of infection and tolerance, of causing a progressive and fatal form of tuberculosis, which was transferable from animal to animal by serial passage. In their feeding experiments, 17 calves, taken from tuberculosis-free herds, were fed with milk from tuberculous cows or cows suspected of being tuberculous. Fourteen were vaccinated and three were controls. The conditions laid down by Calmette and Guérin in their feeding experiments at Gruville were followed as closely as possible. All the animals developed tuberculous lesions.

Rankin, however, thought that his experiments showed that bovines vaccinated with B.C.G. acquired some resistance to a virulent strain. Petroff, Branch and Steenken[9] have carried out experiments in regard to the pathogenicity of B.C.G. for guinea pigs and rabbits and the production of tuberculin allergy, using a strain of micro-organisms received from Dr. E. A. Watson and two obtained from Professor Calmette. They believe that they can get two forms of bacilli from the original material—an "R" form and an "S" form. "R" and "S" are arbitrary designations, meaning "rough" and "smooth", respectively, but the authors prefer to interpret them as meaning "resistant" and "sensitive" to environment. The "S" form is more virulent than the "R", and is able to produce invariably progressive lesions in guinea pigs, and occasionally in rabbits, which usually lead to death. The lesions produced by the "R" strain, however, tend to heal and disappear in from two to four months. The authors further believe that by continuous subculture on potato-bile media Calmette has gradually eliminated most of the "S" colonies, so that the "R" colonies have come to predominate. The virulent "S" colonies, however, have never been completely eradicated, and, under favourable conditions, may increase in number so that reversibility of virulence may take place. Even an "R" colony, when inoculated intravenously, may give rise to a fatal tuberculosis, suggesting either that the "R" colony is not quite free of "S" forms, or that mutation of "R" into "S" may take place in the animal body. If the second theory be correct no one can predict what may happen in course of time when B.C.G. is introduced into the human body, or when it is accidentally carried from person to person, or, again, what transformations may occur after a series of such passages. Furthermore, the immunity produced by B.C.G. is no greater than that produced by organisms killed by heat, and the latter method is potentially less dangerous.

Griffith, furthermore, has been unable to confirm the view of Calmette that the ingestion or inoculation of B.C.G. can give complete protection to monkeys agaínst an infection with virulent tubercle bacilli.

Calmette and Plotz reply to the criticisms of Greenwood and Rosenberg that, at any rate, the statistics published since the original paper of 1927 can hardly be controverted, since they refer to children vaccinated at birth and non-vaccinated subjects, all of whom were born and brought up in tuberculous families and had been followed for a period of four years. They also point out that the results obtained by Petroff and his associates are in complete disaccord with the numèrous experiments carried on at the Pasteur Institute of Paris, the Robert Koch Institute at Berlin, by Kraus and Gerlach at Vienna, by Ascoli at Milan, by Zlatogoroff and Tzeknowitzer at Kharkoff, by Silberschmidt at Zurich, by Cummins at Cardiff, and by Chagas at Rio de Janeiro. No one, except Petroff and his co-workers, has been able to augment the virulence of B.C.G. by animal passage. Calmette and Plotz conclude that B.C.G. represents a fixed, hereditarially attenuated strain. They suggest that Petroff's material had been contaminated with an extraneous virulent strain. The possibility of this Petroff vigorously denies.

In regard to the matter of immunity production the figures given by Calmette and Plotz indicate that the mortality from all causes among unvaccinated children of ages from birth up to four years was 21.4 per cent (of which 15.9 per cent were tuberculous), while the mortality from all causes among the vaccinated children was only 11. 8 per cent (of which 3.4 per cent were tuberculous). These figures were ob-

9. PETROFF, S. A., BRANCH, A., and STEENKEN, JR. W., *Am. Res. of Tuber.* **19:** 9, January, 1929.

tained from 2,368 vaccinated and 4,854 non-vaccinated children, born and brought up in tuberculous families. It has further been shown that where vaccination with B.C.G. has been systematically practised over a period of years, as has been done in certain French and Roumanian cities, the general mortality has been reduced to about one-half and sometimes to two-thirds. In France alone 132,000 have been vaccinated from July, 1924, to January, 1929. In no case has a harmful result followed the use of B.C.G. All this is evidence that B.C.G. is efficacious and inoffensive.

Summing up, it is clear that the clinical observers support Calmette's conclusions, while some, at least, of the laboratory workers have their doubts. It seems but fair to say, in weighing the pros and cons of this question, that guinea pigs, rabbits and monkeys are hardly the equivalent of human beings. Valuable information as to the harmlessness or otherwise of B.C.G. for mankind would be obtained from post-mortem examinations in the case of vaccinated persons dying from various causes. Limited observations along this line are lately available. Dr. and Mme. Zeyland[11] in a study of fifty autopsies on children vaccinated with B.C.G., who had died of non-tuberculous disorders, found that the bacillus had been able to penetrate the wall of the intestine without producing local lesions and that acid-fast organisms could be recovered from the mesenteric lymph-nodes, which when injected into guinea pigs proved to be non-virulent. Their observations were to the effect that B.C.G. is harmless and does not produce the lesions of tuberculosis under the conditions of immunization, *i.e.*, where the vaccine has been given by the mouth, either in the case of normal children or of those who are premature and feeble. The number of cases studied by these observers is too small to finally settle the point, but it is to be hoped that further studies of this kind will be made. And so the matter rests.

A.G.N.

11. ZEYLAND, J., and PIASECKA-ZEYLAND, E. *Ann. d. l'Inst. Pasteur* **43**: 767, June, 1929.

## THE ADEQUATE PROVISION OF VITAMINS

IN no department of preventive medicine has more progress been made during recent years than in that of nutrition, which we now recognize as closely dependent, not only upon the character of our food but also on the presence in it of the several vitamins in efficient amounts.

An imperfect appreciation of the importance of fresh fruits and vegetables in the daily dietary developed during the seventeenth century, but made slow progress through the eighteenth and nineteenth centuries, though it must have been stimulated by the frequent breaking out in epidemic form of one of the many deficiency diseases as we now know them. Scurvy was the first one recognized as such, and led to distressful disease and death among our pioneering sailors on their long voyages, and among early settlers in new colonies during the long winter months when all fresh foods failed.

Not until the second decade of the present century did biologists become aware of how essentially important to the nutritive power of food was the presence in it of the minute chemical substances at first termed accessory food factors, but which later on, with more knowledge, received the name of vitamins.

Persistent research since than has converted the subject of nutrition into a science applicable to general use, and although our knowledge regarding these vitamins is by no means complete, we have at present sufficient facts to guide and aid us in attaining more perfect methods of nutrition than were reached in the past century.

The knowledge we have so recently gained regarding the importance of vitamins is especially valuable to us in the preparation of a suitable artificial food for the rapidly developing infant. Too frequently have the disastrous effects on nutrition, which develop in important tissues of the infant when any of the special vitamins are lacking, had a practical demonstration.

We desire, therefore, to call special attention to the article in this issue in which Dr. Tisdall and his co-workers after discussing the various mineral ingredients and vita-

mins necessary to the nutrition of an infant describe a whole wheat biscuit which is now being placed on the market, and which has been prepared under his special supervision.

Regarding these vitamins, it is unfortunate that they exist in foods in such minute amounts, that chemists and biologists have found difficulty in extracting them and measuring their efficiency. As a rule feeding experiments on small animals have to be made to determine their presence and judge of their quantitative efficiency. We do know, however, that each vitamin appears to have its special field of action in the economy. One vitamin cannot be substituted for another. Each must be considered individually, and all of them must be present in an effective amount to secure perfect nutrition. Dr. Tisdall states that these biscuits supply not only the mineral constituents that research has shown to be necessary in an artificial food for infants, but also many of the vitamins. Nevertheless, we think him wise in emphasizing the administration of cod liver oil in addition to the employment of these biscuits in the artificial food daily given to the infant. We also think it wise that, in addition to the cod liver oil with its vitamins A and D, an effective amount of vitamin C should be administered daily in the form of fresh orange juice, ripe tomato juice, or possibly, as recommended by Dr. Eddy of Boston, some ripe banana flour, lest lacking this vitamin the development of good dentine in the teeth of the growing infant should be checked. All the more is this the case as vitamin C appears to be more susceptible than some of the other vitamins to a slow oxidation by age and by repeated heatings. These, however, are simple additions easily made, and we can confidently recommend these biscuits to the consideration of pædiatricians and physicians who have to arrange for the artificial feeding of infants and young children.

A.D.B.

## THE ZONDEK-ASCHEIM TEST FOR PREGNANCY

FOR years, indeed from all time, there has been need for a reliable diagnostic test for pregnancy, particularly for pregnancy in its earliest days. We used to be told that "Time is the great diagnostician," and this aphorism certainly found its application in the matter of pregnancy. But, cases not infrequently arise in which a final conclusion would be welcome, and in which the aphorism affords but cold comfort. At length, however, it would seem that a test for pregnancy has been devised, which, while it is not absolute is so nearly so as to be of enormous value. We refer to the Zondek-Ascheim reaction.

Zondek and Ascheim[1], in 1927 showed that the implantation of pituitary tissue, whether from the male or female, into immature female mice produced precocious sexual maturity. The most notable evidences of this were: (1) canalization of the vagina; (2) the appearance of œstrus, as inferred from the vaginal smear; (3) hyperæmia and enlargement of the uterus; (4) enlargement of the ovaries, with the appearance of hæmorrhagic spots. The changes in the ovaries are worth describing in somewhat fuller detail. The hæmorrhagic spots ("corpora hæmorrhagica" of Zondek and Ascheim) proved to be unruptured follicles into which blood had poured; the follicles had, in fact, ripened. Besides this, a number of corpora lutea can be seen, some of which contain a degenerating ovum. These are called "corpora lutea atretica."

Following up their experiments, Zondek and Ascheim[2,3,4] later discovered a hormone in the urine of pregnant women, which, when injected into immature female mice, produced effects closely resembling those caused by the implantation of pituitary tissue. The urine of non-pregnant women had no such effect. This observation constitutes the Zondek-Ascheim test.

A test of such importance and probable value naturally attracted a good deal of attention, and Zondek and Ascheim's work has been repeated by several workers,

1. ZONDEK, B., and ASCHEIM, S. *Klin. Wchnschr.* **6:** 248, 1927.
2. ZONDEK, B., and ASCHEIM, S. *ibid.* **7:** 831, 1928.
3. ZONDEK, B. *Klin. Wchnschr.* **7:** 1401, 1928.
4. ASCHEIM, S. *Klin. Wchnschr.* **7:** 1453, 1928: *Zeitschr. f. ärtzl. Fortbild.* **26:** 5, 1929.

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notably by Brühl[5], Philipp[6], and Allan and Dickens[7]. It may be said at once that Zondek and Ascheim's observations have been amply confirmed, and that their test is to be regarded as of great value.

Brühl obtained a positive reaction in 67 out of 68 pregnant women, in all of six cases of tubal pregnancy, and also with the urine of a woman six weeks after confinement. He concluded that a positive result with the Zondek-Ascheim test is a conclusive indication of the existence of pregnancy, and that a negative result excludes pregnancy with absolute certainty. Brühl seems to be unduly enthusiastic, however, for he obtained positive reactions in one case of leucorrhœa with erosion of the cervix, three cases of colpitis (kraurosis), four cases of climacteric disorders, and seven cases of malignant disease of the genitalia.

Repeating Zondek and Ascheim's work, with slight modifications, on 208 pregnant and 29 non-pregnant women, Allan and Dickens obtained only five incorrect results. One woman at the menopause gave a positive reaction and four normally pregnant women gave negatives. They conclude, therefore, that in the human subject the test may be relied upon with some confidence, the percentage of error being low for such a reaction. In the case of women definitely known to be pregnant the percentage of error was only 3.2, and in those definitely known not to be pregnant it was 1.2.

Very similar results have been obtained by other workers, notably those at the Courtauld Institute of Biochemistry of the Middlesex Hospital, under Prof. E. C. Dodds. In these particular experiments, out of 126 women known to be pregnant 122 gave a positive reaction while only 1 out of 82 non-pregnant women did so.

The explanation of the discrepancies is not yet forthcoming. With regard to the positive reactions at the climacteric it should be noted that these only occur occasionally and then are but feeble. Allan and Dickens suggest, in line with the observations of Fluhmann[8], who showed that after castration, natural or artificial, increased amounts of the anterior pituitary hormone are to be found in the person's blood, that in their particular case an amount of hormone was excreted into the urine sufficient to give a weakly positive test.

The nature of the hormone involved is still under discussiion though there seems to be little doubt that it is derived from the anterior lobe of the pituitary body, as Zondek and Ascheim contend. A somewhat similar hormone, "folliculin" or "oestrin", has been found in the urine of infants of both sexes of from one to ten days old, which, according to E. Philipp (*loc. cit.*), when injected into infantile female mice bring about the changes in the ovary that Zondek and Ascheim consider the criteria for a positive test. This hormone is apparently produced, for the most part, in the placenta, and is also abundant in the liquor amnii, hydatidiform moles, and the fetal blood. Philipp thinks that the pregnancy reaction of Zondek and Ascheim is due less to an overproduction of hormone by the anterior lobe of the hypophysis than to a new production of hormone by fetal tissues. While admitting that oestrin has an effect on the developing uterus and vagina, others deny that it produces the effects on the ovary that Zondek and Ascheim have described. One very important difference between the two hormones in question is that, unlike oestrin, the hormone of Zondek and Ascheim appears early in pregnancy. Allan and Dickens cite one of their cases in which they obtained a strongly positive reaction as early as nine days after a menstrual period was missed. Incidentally, it may be remarked, the early appearance of a positive Zondek-Ascheim test adds greatly to its value. In favour of the hypothesis that the Zondek-Ascheim hormone is derived from the hypophysis, and from its anterior lobe, is the well-established fact that certain well-defined histological changes, together with hypertrophy, occur in the gland during pregnancy, suggesting accelerated action. In one of Allan and Dickens' cases, in which skiagrams showed the presence of a tumour of the

5. BRÜHL, R. *Deutsche med. Wchnschr.* **53**: 696, April 26, 1929.

6. PHILIPP, E. *Zentralbl. f. Gynakol.* **53**: 2386, Sept. 21, 1929.

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posterior lobe, the reaction was negative. Furthermore, the injection of 0.2 c.c. of the hormone of the anterior lobe of the pituitary body, when injected into the skin of a pregnant woman, produces no reaction, whereas, when injected in the same way in the non-pregnant woman a distinct red circle is produced in a few hours, which persists from twenty-four to thirty-six hours.

The accumulated evidence, therefore, goes to show that the hormone responsible for the Zondek-Ascheim reaction is derived from the anterior lobe of the pituitary body; that the reaction is positive quite early in pregnancy, at a time when such positive evidence is most needed; and that the reliability of the test is very high.

It is regrettable that from its nature the test cannot be made generally available. It requires the assistance of a laboratory where a large stock of young female mice is constantly at hand, and where there are trained observers. The test, as a consequence, is expensive. It may prove, however, that the skin test referred to may overcome the difficulty. Recently, Drs. Otto Pollatschek and R. Porges, of Vienna, have made some valuable observations on this phase of the subject, and report that in their hands the skin test has proved to be reliable, except in one patient who had a hypophyseal tumour. Should these observations be confirmed we shall have at last a simple and reliable method of determining the existence of early pregnancy.

A.G.N.

## ASBESTOSIS

ASBESTOS is a mineral of interest to Canadian physicians, particularly to physicians practising in the Province of Quebec, for a very considerable part of the world's supply of asbestos is mined in the Black Lake District between Quebec City and Sherbrooke. If work with asbestos presented a hazard to the worker it would be reasonable to suppose that cases of disease would be reported from time to time, but so far as can be determined no cases of specific disease have been reported among asbestos workers in the Province of Quebec. This does not mean, however, that a hazard does not exist; it merely means that no hazard has been recognized.

Mortality and morbidity records of asbestos workers are not available. In fact, information as to the effect of such work on the worker is extremely limited. The death of an asbestos worker which occurred in 1900 was reported by Dr. Murray in England to the Department on Industrial Diseases, and the evidence suggested that the death was due to an occupational disease. This case was not reported in the medical literature. No further reports appeared until 1924, when Dr. W. E. Cooke, of the Wigan Infirmary, published the history of a case of pulmonary asbestosis. Since then a number of isolated cases have been reported, mostly in the manufacture of asbestos, and mostly in England, but four cases in Southern Rhodesia were reported by R. W. Simson in 1928. The latest publication on the subject is by W. E. Cooke, in the *British Medical Journal* for September 28th, 1929. This article is in the nature of a review.

Asbestos occurs in nature as a fibrous form of serpentine. Its analysis varies somewhat in different parts of the world, but it is essentially a magnesium silicate. There may or may not be iron present, and some forms contain aluminum. The Canadian asbestos is said to contain about 41 per cent of silica and 2.5 per cent of iron oxide.

Clinically, asbestos affects two tissues. First, it may produce small warty growths in the skin,—the so-called "asbestos corns." Secondly, it may give rise to a fibrosis of the lungs, somewhat similar to that produced by silica. Investigation of the "asbestos corns" indicates that they are granulomatous in nature and have for their core a tiny spicule of asbestos fibre. Evidently asbestos is mildly irritating to the body tissues. The manner of the formation of the pulmonary lesion is of great interest to students of pneumoconiosis, for there is a widespread impression that silica is necessary to the formation of pulmonary fibrosis. Nor can it be said at present that this view is definitely disproved by the occurrence of pulmonary asbestosis, since asbestos in itself

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is a silicate. To our knowledge no analyses of pulmonary tissue for silica have been made in cases of asbestosis.

It might be thought that the lesion in this condition was essentially the same as that of ordinary silicosis, if it were not for the fact that certain very characteristic bodies are reported unlike those seen in any other pathological picture. We refer to the so-called "curious bodies." Microscopic sections of lungs of asbestos workers show large elongated bodies varying in length from 10 to 100 microns. They may have single clubbed ends or may appear as elongated dumb-bells, and sometimes single coccal or streptococcal forms are seen. These bodies do not stain with the ordinary aniline dyes, but are themselves pale yellow or yellowish brown. The "curious bodies" may be isolated from lung tissue by digesting portions of the lung with trypsin. They may then be teased out, and in this way some idea of their structure may be obtained. Apparently they are composed of a central core, which is probably an asbestos spicule, upon which colloidal aggregates of blood proteins have been adsorbed. These "curious bodies" have been reported in different places in England and South Africa; in fact every published report of pulmonary asbestosis has described them. 'It is the opinion of Dr. Cooke that the 'curious bodies" are diagnostic of pulmonary asbestosis.

Since the reported cases of this disease have occurred largely among weavers and spinners it is possible that the mining and crushing of asbestos does not present a hazard. The failure to recognize the disease in Canada, however, is no evidence of this, for in other occupations experience has shown that large groups of men may suffer serious occupational effects, which go unrecognized for years. FRANK G. PEDLEY.

## Editorial Comments

### LE MAL DES CRÈCHES

The problem of the crèche or foundling hospital is how to lessen the relatively high rate of mortality that so often exists among the children cared for in these institutions. The death rate, formerly nothing less than appalling, has been of late much improved through a fuller appreciation of the value of pasteurization of milk and of the decisive part played by vitamins, but it is still too high. The outstanding features of the affection that carries off so many infants, as is well known, are athrepsia and diarrhœa. This affection can hardly be termed a disease, as it is not a single entity and the causes are multiple. Yet many names have been applied to it—le mal des crèches, summer diarrhœa, infantile cholera, milk injury (Czerny), disturbance of equilibrium (Finkelstein), and some others. Actually, what is called by these various names is a symptomatic condition with a varied etiology.

Drs. Longpré and Panneton, in a helpful article that appears in the present issue of the *Journal,* have done good service in emphasizing one important cause at least, namely, infection in the nose, throat, and ear, an infection, moreover, which may be diphtherial and, as such, unsuspected. These authors point out that the problem involved, in many cases at least, is one of infection rather than alimentation. Careful examination, of the nose, throat, and ears, both clinical and bacteriological, should be carried out in all infants that are not thriving, for lesions of these organs may be overlooked or, on account of their relative benignity, may be passed over as of little account.

Drs. Longpré and Panneton give some striking figures as a result of their investigations in a crèche with which they are connected, though they do not claim that their findings are necessarily applicable to other similar institutions. In sixty autopsies conducted on children dying with the "mal des crèches" only two infants were found to have intestinal lesions. The outstanding conditions found were otitis and mastoiditis, which were present in fifty cases. Without eliminating completely frank gastro-enteritis, their experience leads them to think that the signs manifested in the digestive tract in cases of athrepsia are not primary but secondary to a septicæmia, usually due to infection in the ear. Furthermore, the authors have examined, in 151 cases, the secretions from the nose and throat in patients manifesting no local symptoms, and the pus in cases of otitis, and were surprised to obtain *b. diphtheriæ* in 85, or 56.3 per cent. Of course, the discovery of *b. diphtheriæ* in noses and throats that do not manifest the typical signs of diphtheria, or, indeed, any signs at all, is not new, but Drs. Longpré and Panneton have performed a useful service in pointing out an important cause of trouble in hospitals for children, where the diets prescribed are proper, and the care is otherwise beyond reproach.

A.G.N.

### AUTOMOBILE FATALITIES IN 1929

The Metropolitan Life Insurance Company sounds a warning note in pointing out in its statistical bulletin for November, 1930, that the cumulative death rate from automobile accidents for the first ten months of 1929 was 19.5 per 100,000, the highest ever recorded. This represents an increase of 11 per cent in the United States over that of a similar period in 1928, and an increase of 25 per cent in Canada. One-third of all accidental deaths of policy-holders were due to this cause, and it is now the only type of fatal accident which is increasing in both countries. More than 2 per cent of all deaths are now caused by automobile accidents, and among Metropolitan policy holders such accidents have caused more deaths than measles, whooping cough, scarlet fever, and diphtheria combined. Things seem to be quite as bad elsewhere. According to Mr. Herbert Morrison, Minister of Transport, London has the worst record for traffic fatalities of any of the world's capitals. It is reported that no less than ninety-eight persons were killed during the first two weeks of January of this year alone. In 1928 one pedestrian in every ten thousand was killed in the streets of London, while in Paris the proportion was much less, only one in twenty-five thousand. During 1929 the Londoners were killed off thrice as fast as the Parisians. Apparently the laws should be made more stringent over there, for we understand that in England motor drivers are not subjected to any tests of knowledge or efficiency. It may be said, however, that it is questionable whether the most carefully devised laws will be sufficient to do away with road accidents. What seems to be needed, perhaps more, are care, courtesy, and common sense. This applies to pedestrians as well as motorists.

R. VANCE WARD

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### ROYAL COLLEGE OF SURGEONS OF ENGLAND

*Primary Examinations in Montreal, September, 1930*

Following upon the successful outcome of the examination, held for the first time outside of London, in Toronto last August, the Council of the Royal College has agreed to conduct the examination in Montreal this coming September.

The same procedure will be adopted, *viz*: two examiners in each subject, Anatomy and Physiology will be sent from England, and one assessor in each subject will be appointed by the Royal College from those qualified and resident in Canada.

Inasmuch as the expenses incident to the examination are extremely heavy, the holding of the examination is dependent upon a sufficient number of candidates presenting themselves, and it has been found necessary to establish a rule whereby a candidate whose Entrance Form is accepted and who is declared eligible shall forfeit one-half of the fee if he fails to present himself at the time of examination.

For the examinations last year thirty-seven candidates were accepted; only twenty-three paid their fees and sat. There was, therefore, a considerable deficit which was borne by the Royal College. Against a repetition of this these protective measures must be taken.

A detailed announcement of the forthcoming examination in Montreal will be found on page xviii of this issue, under advertising matter.

A.T.B.

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### MAJOR-GENERAL SIR WILLIAM GRANT MACPHERSON, C.B., K.C.M.G., LL.D.

The death of Major-General Sir W. G. Macpherson, colonel-commandant of the Royal Army Medical Corps, which occurred in October, 1927, marked the loss of a medical officer of great distinction and one well known to many Canadians. On December 8, 1929, the officers of the Royal Army Medical Corps recalled his memory very fittingly by the dedication of a bronze tablet on the north wall of St. Giles' Cathedral, Edinburgh, "in humble gratitude for his great and distinguished service."

Sir William was popularly known as "Tiger Mac," a name not given him on account of anything ferocious or daring in his character, but as a tribute of his energy, thoroughness, and singleness of purpose. During the War he was mentioned nine times in despatches, and received honours from France, Italy, and the United States. Probably his most lasting title to remembrance will consist in the fact that he was the able and faithful historian of the Great War. His "Medical History of the War" is the official record of the medical service during that stirring period, and is known to many as an accurate and comprehensive work.

A.G.N.

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### A REQUEST FOR CUSTOMS TARIFF EXEMPTION ON MEDICAL BOOKS

At the present time medical books enter Canada under tariff item 171 and are dutiable, being charged 5 per cent British Preferential Tariff and 10 per cent General Tariff. This does not seem logical, as the question of health is one of paramount national importance and nothing should be permitted which would impede in the slightest degree the dissemination of medical knowledge. In the science of medicine there are no national boundaries and each medical discovery soon becomes the property of all.

It is obvious that such a tariff cannot act as

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a protective duty for all medical discoveries do not originate in Canada, despite the fact that Canada can boast of contributing a remarkably full share. Medical knowledge, or, more correctly, medical progress, is not a commercial commodity which can be turned out, factory-fashion, for local consumption only.

The government recognizes this principle in that books not printed in Canada which are used as text-books by medical schools are permitted free entry, as are also books purchased for incorporated medical societies and libraries and not the property of individuals. These provisions, however, are of little help to the practitioner of medicine or to the research worker for various reasons. Many publications are too advanced to be considered as textbooks in medical schools; only a limited few of the many excellent medical works available can be listed for student use; the new books and publications which are most eagerly sought by the progressive practitioner or research worker do not appear in the university calendars for some time; and an incorporated medical library, even should it contain the desired volume, may not be close enough to benefit the doctor or the individual most concerned, the patient.

While we prefer Canadians to contribute articles to our own medical publications, it can but be expected that highly technical contributions are more likely to reach the individuals most interested if appearing in those journals maintained for the consideration of certain clinical and research specialty groups. In such instances, reprints of these articles sent to Canadian contributors are now dutiable.

The burden of the present tariff arrangement falls not only upon the medical profession but upon chemists, engineers, metallurgists and others, as this part of item 172 now limits free entry to books dealing with *application* of science to *industries*, thus not covering purely scientific, professional or non-commercial publications. Accordingly, the Canadian Institute of Chemistry, the Canadian Institute of Mining and Metallurgy, the Engineering Institute of Canada and the Canadian Medical Association have requested a revision of item 172 to provide free entry not only for scientific books directly related to industry but to books relating to any science or scientific process whether commercial or not; to works on biology, chemistry, geology, mathematics, medicine, nursing, physiology, laboratory technique or any branch of pure or applied science; reprints on scientific subjects, medical or scientific dictionaries and scientific reference books of all kinds; to mention but a few of the additions suggested for the redrafting of this particular item. We understand that this brief will be reviewed by the Tariff and Taxation Board, and, if favourably considered by this Board and the Minister of Finance, will go on to the House this session.

G. HARVEY AGNEW

## THE OVARY-STIMULATING HORMONE OF THE PLACENTA

We direct attention to a short series of papers in this issue by Drs. Collip and Campbell, which are of unusual interest. They contain the first notice of some work on the subject of a standardized placental extract capable of influencing the ovarian function in a definite degree. The search for such a hormone has been assiduous and prolonged. That it existed in the placenta had been shown by other workers, but its extraction in a form in which its effects could be properly controlled had been a baffling problem. Dr. Collip has now been able to prepare a placental extract which can be administered by mouth. This extract has produced in animals results which suggest therapeutic applications in human beings, and the tentative conclusions of the authors on this latter aspect point to great possibilities. As they remind us, the series of cases is small, but the results obtained are apparently impressive.

We look forward with interest to further communications on this subject. H.E.M.

## A CORRECTION

We regret to say that in our last issue an error was made in referring to the Osler Library at McGill University. The library was spoken of (*vide* Men & Books, introductory note to Garrison's book review) as the "Osler Memorial Library." We have been asked to say that this should be the "Osler Library." It is actually Sir William Osler's library, not one dedicated as a memorial to him.

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THE SEDIMENTATION TEST IN DIABETES MELLITUS—Wisselinck has performed a series of investigations on patients with diabetes mellitus to ascertain what effect the amount of sugar in the blood and urine, ketonuria, and insulin had on the sedimentation rate of red blood corpuscles, since other workers had obtained conflicting results. Westergren's technique and normal standards were adopted and over 300 tests were made on 63 diabetics. In 25 of these the sedimentation rate was normal; in some of the remainder it was increased, and in others diminished. Wisselinck came to the conclusion that on the whole the rate was independent of the clinical condition in diabetes, that the amount of sugar in the blood and urine and the administration of insulin had no constant effect on the rate, and that it was of no prognostic value in diabetes mellitus.—*Münch. med. Woch.*, p. 1373, August 16, 1929.

# Special Articles

## EXTREME HYPOTHERMIA IN VARIOUS ANIMALS AND IN MAN

### WITH NOTES ON THE DETECTION OF LIFE AND THE POSSIBILITY OF RECOVERY IN CASES OF APPARENT DEATH FROM EXPOSURE TO COLD

BY S. W. BRITTON, B.Sc., M.D., C.M. (McGill),

*Professor of Physiology, University of Virginia, University, Va.*

From the returns given by vital statistics during the past few years it is evident that death from exposure to cold is a fairly common occurrence in countries situated within the North Temperate Zone. In the various territories of the United States, for example, the mortalities from excessive cold have ranged between two and four hundred per year for many years past. It is also well known that a large number of people similarly meet death every year in different parts of Canada. This is clearly shown by the annual Provincial returns, though definite numerical data for the whole Dominion are not available. Of the two extremes of temperature, indeed, it is obvious that man's chief enemy is cold, and, futhermore, if the physical fate of the earth be correctly predicted, this fact must become more pronounced with the passing of time and the coming of later generations.

The present paper deals briefly with a few of the earlier known facts with regard to low temperatures observed in some of the lower types of organisms, and at greater length with some of the more recent observations on those higher animals which normally possess uniform or only slightly varying body temperatures characteristic of elevation of type, and which may thus be very reasonably compared with man in their response to the induction of severe hypothermia. The influence of glandular secretions on body temperature regulation is also discussed. Several instances of extremely subnormal temperatures in man are quoted, and suggestions are presented on the determination of the presence of life and possible recovery in cases where the hand of death may ordinarily appear to have long since passed.

#### POIKILOTHERMIC ANIMALS AND LOW TEMPERATURES

Some of the lower poikilothermic forms of animal life show remarkable ability to withstand low temperatures. The Arctic explorer Ross[1] repeatedly froze and revived caterpillars (*Laria rossi*), reaching a minimal temperature of –42°C. Other observers have shown that various species of insects survive exposure to a temperature of 40°C. below zero, with no apparent ill effects following. John Hunter[2] found that the body temperature of a fish such as an eel could be reduced to approximately O°C., and that, though at first it appeared to be dead, recovery took place when the temperature of the surrounding water was raised. Goldfish which were apparently frozen used to be exhibited by Pictet[3] at his lectures, and these could sometimes be revived on gradual thawing.

Frequently in these earlier experiments, however, no very definite records of body temperatures and of general and specific reactions are available. In order to determine with more precison, therefore, the lower temperature limits at which varying types of fishes may still maintain life, and also to observe the effects of extreme temperatures on heart and respiratory rates, on reflex action and on general behaviour, a series of experiments was undertaken by the writer[4] at the Atlantic Biological Station at St. Andrew's, N.B. Briefly, it was shown that fishes could survive exposure to sea water at temperatures from one to almost two degrees below zero for several hours; many reflexes could be elicited during this period, but gradually all vital activities disappeared, and the heart-beat itself was eventually arrested. The body temperature of such fishes (many widely differing species were used) now approximated that of the surroundings; they appeared to be stiffly frozen, and on ordinary observation altogether lifeless. On increasing the temperature of the surrounding water, however, in the course of only a short time, complete resuscitation to normal activity was found to occur.

A particular "order of recovery" has, moreover, been observed in extremely cooled fishes. The heart-beat at first appears, on slight elevation of body temperature, followed by the occurrence of various appendage reflexes, the respiratory reflex (on anal or pectoral stimulation), and, later, by normal respiration, vision, equilibration and natation. It was also shown that the heart of a fish could be frozen for several hours at a temperature of –20° C. and yet, on slowly thawing, recover its normal rhythm. In the cooling of fishes, the heart-beat and the respiratory rates were found to vary according to the body temperature. (See also reference 5.)

It is commonly believed that frogs are often "frozen solid" for long periods during their winter sleep, and still survive, but recent observations fail to substantiate this belief. Cameron and Brownlee[6], for example, in a number of experiments, show that *Rana pipiens* and similar species do not sustain life on the lowering of their body temperature to –1.25° C. for more than one hour.

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### HYPOTHERMIA IN HIBERNATING FORMS

On the approach of winter certain types of animals retire to their burrows or other shelter, become inactive, and fall into a torpid state. All the activities of the body are greatly reduced, and the temperature generally falls to a point only slightly above that of the surroundings, which, however, is usually several degrees above 0° C. This phenomenon of hibernation is found to occur in many classes of animals, including mammals, reptiles, amphibians, insects, molluscs and probably fishes, but no cases amongst birds have been recorded. The etiological factors connected with winter sleep appear to be not yet definitely established. Hibernating animals are found to emerge spontaneously from their torpor in spring, however, when food supplies are usually available and climatic conditions are more favourable; nutritional economy and environment have therefore been urged by many as the most important considerations.

The attention of many investigators (Walther, Horvath, and others) has, at various times, been directed towards the study of hypothermia in hibernating animals. With a view to studying the reactions of such animals at low temperatures under adequate control, Tait and Britton[7] carried out a number of artificial cooling experiments on the common North American woodchuck. It was found that in some instances the body temperature could be reduced to the extremely low limit of 0°C., at which level the respiration and heart-beat were scarcely if at all perceptible by ordinary means, and the blood pressure, taken with a mercury manometer in the carotid artery, showed a fall of mercury to practically zero from a normal for the animal of about 100 mm of mercury. In several cases respiration really failed before the body temperature reached 0° C., and then artificial respiration was supplied at occasional intervals, while cooling was pushed still further.

It was shown that such severely-cooled animals could be readily resuscitated by artificial warming of the whole body, or in extreme cases by an initial direct application of warm Ringer-Locke solution to the failing, or even to the already stopped, heart. Recovery of the woodchuck was found to occur *spontaneously* after artificially cooling the animal to a deep rectal or œsophageal temperature of 3°C.

Observations which have recently been made by Johnson[8] indicate that body temperatures approximating 0° C. may be found in the ground squirrel during the period of torpidity. Tait[9] also has pointed out that certain excised tissues, particularly the heart, of hibernating animals may continue in activity at very low temperatures. Whereas the excised heart of an ordinary mammal ceases to beat at about 17° C., the heart of a woodchuck is not arrested by any temperature short of freezing.

### HOMOIOTHERMIC ANIMALS AND EXPOSURE TO COLD

The influence of low temperatures on true homoiothermic animals was first systematically investigated in the laboratory by Walther[10]. Experimenting with immobilized, non-narcotized rabbits, he found that cooling to a temperature of 20° C. abolished the capacity for spontaneous recovery of the normal body heat, and that artificial warming was necessary in order to effect complete restoration. Cooling below 20° C., he believed, inevitably led to death.

In a series of four experiments on monkeys, Simpson[11] succeeded with the help of anæsthesia in reducing the body temperature of one animal to the low level of 14° C., and in subsequently reviving it by artificial warming. Three other animals similarly exposed to cold did not survive. Further investigation of the condition of cooled animals was made by Simpson and Herring[12], who used cats in their experiments. They stated that at 24° C. the function of the heat-regulating mechanism was suppressed. A temperature of 16° C. was found to be the lowest limit at which cats still showed evidences of life.

That true homoiothermic (non-hibernating) mammals do possess a heat-regulating mechanism which is wonderfully well adapted for dealing with extremely low body temperatures has now been made clear (Britton[13]). Working usually with cats, possessing normally a temperature of 38° C., it was found that cooling really induced a progressive paralysis of the central nervous system. Consciousness disappeared, for instance, at 27° C., the pupillary reflex to light was abolished at 23° C., and shivering was suppressed at 20° C. Of particular interest is the fact that the knee-jerk almost constantly, and one or two other reflexes occasionally, persisted until both rectal and œsophageal thermometers registered only 16° C. In such cases of severe hypothermia the skin and immediate subcutaneous tissues were several degrees colder, and the extremities in some instances were frozen. Both the pulse and apex beat were usually impalpable, and respiratory movements occurred only one to five times per minute, and were sometimes scarcely perceptible; the eyes were half open, the cornea was dull and the pupil usually dilated; the tongue protruded, and the skeletal musculature showed a condition of flaccidity, unless the parts had been really frozen. The animal could be said to be in a state of extreme cold narcosis, since nociceptive stimuli were ineffective, and surgical procedures could be carried on without arousing the least indication of resistance. The presence of the knee-jerk, therefore, and occasionally the anal sphincter (dilatation) reflex on respiration, constituted important signs of life, when on ordinary observation the pronouncement of death would have been made. It may be mentioned that in many particulars the effects of gradual cooling showed a strong similarity to those produced by the induction of anæsthesia.

At the extremely low body temperature of 16° C., artificial warming was necessary in order to effect complete resuscitation of the animal. This was found to be best accomplished by the administration of warm and, later, hot water baths, accompanied by artificial respiration as demanded by the animal's condition. No particularly ill results were apparent in those animals which were revived from the most extreme cold narcosis (14° to 16° C.). The administration of ordinary therapeutic doses of such drugs as strychnine and alcohol had practically no effect on the cooled animal, probably because of the very slow rate of absorption by the tissues.

It is particularly noteworthy that a definite thermogenic ability is retained by the highly differentiated animal organism even when it is reduced to the low body temperature of 19° C. The activities of the heart, respiratory muscles, and abdominal viscera, although markedly diminished at this severely subnormal temperature level, are probably wholly responsible for the first small rise in body temperature, even against a *lower* external temperature. Naturally initiated shivering and stepping movements, and an exaggerated muscular tonicity which occurred later, ensured eventual recovery of the animal. A number of artificially-cooled cats showed perfect spontaneous recovery from body temperatures of 19° C. or 20° C. It has also been shown that other homoiothermic animals, including guinea-pigs and dogs, may sustain life, and be recovered from similar remarkably low body temperatures, with no ill effects ensuing. Some further details relating particularly to the heat-regulating mechanism of mammals may be consulted in an article by Barbour[14]. The recent monograph by Pearse and Hall[15] is also exceedingly instructive.

## EXTREME HYPOTHERMIA IN MAN

Although the normal variation of body temperature in man is usually within 1° C., many striking differences have been observed in cases of exposure to an excessively cold environment. In some instances the temperature has fallen to approximately 24° C. without a fatal issue. Similar to those conditions occurring in other animals, in man this fall of temperature is accompanied by paralysis of the highest nerve centres and loss of consciousness. The centres in the medulla are later affected, so that respiration is slowed, and the blood pressure falls concurrently with a drop in the pulse rate.

Reincke[16] has recorded numerous cases of hypothermia resulting from the accidental exposure of drunkards to cold air and water. In two individuals the rectal temperature was 30° C. and 24° C., respectively; the patients were unconscious, but under treatment recovered in a day or two. In other cases, with temperatures of 28.4° C., 27° C. and 26.4° C., death followed in about 24 hours. In a case observed by Nicolaysen[17] the rectal temperature was 24.7° C., but the inebriate, who had been exposed the whole night to air at about 6° C. below zero, completely recovered. The temperature of the vagina was 27.9° C. in a woman (quoted by Peter[18]) who had a similar experience; under treatment the temperature rose to 36.3° C. within six hours, and the patient completely recovered.

Weiland[19] has recorded two cases of adults with temperatures reduced to 28.4° C. and 26.6° C. from exposure to cold, the determinations being taken by the rectum several hours before death. In a third case, that of an individual who had been exposed to cold while under the influence of liquor, the rectal temperature was 30.4° C., and yet recovery took place. An observation of a body temperature of 26.7° C. in a man who still retained consciousness was made by Tigerstedt[20] who also discusses other cases in which recovery was made from 24° C. Kohler[21] noted a temperature of 28.2° C. in the rectum of a drunkard, and found that, notwithstanding treatment, it remained low until shortly before the man's death a month later.

In four cases of insanity observed by Lowenhardt[22] the patients often ran about naked in cold weather, and body temperatures as low as 25° C., 29.5° C., 23.7° C. and 28° C. were recorded; in one case the range of temperature for several weeks was from 25° C. to 35° C. All the patients were about sixty years of age; although fairly active they did not take much food, and appeared well.

Recovery in cases of exposure while under alcoholic influence would depend in large measure, of course, on the amount of alcohol taken and the individual resistance, as well as on the particular degree of cooling of the organism. That glandular mechanisms are highly important in connection with the general factor of "individual resistance" is very apparent from what is now to be considered.

## GLANDULAR INFLUENCES AND TEMPERATURE REGULATION

A number of workers (see Cushing and Goetsch[23]) have considered that the pituitary gland is of importance in connection with the regulation of body temperature. The results of others[24], [25] are not wholly in accord with this viewpoint, however. That the so-called hibernating gland (*la masse hibernale*) may be a significant factor in relation to winter sleep has also been mooted[26]. Pathological conditions of the thyroid gland, too, have long been known to produce marked effects on oxidative processes, and therefore on thermal regulation in the organism.

The recent observations by Finney, Dworkin, and Cassidy[27] are of distinct significance. They noted that a condition simulating hibernation could be induced in various animals by the combined action of cold and insulin, and that adrenalin and pituitrin readily restored the shivering reflex in cooled animals. Very low respiratory quotients were found during the state of artificial hibernation.

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Recent evidence has been presented (Cannon, Querido, Britton and Bright[28]) which indicates that the secretion of the adrenal medulla is very definitely linked up with the chemical control of body temperature. By establishing a known "heat debt" (measured by c.c. of ice water given by stomach tube per kilo weight of animal) it was observed, with the use of the denervated heart of the animal as an indicator, that marked secretion from the adrenal medullary tissues occurred during the discharge of the "debt;" furthermore, similar results were forthcoming on exposure of animals to cold surroundings. Metabolism experiments on man, too, were corroborative of the foregoing. Adrenin secretion probably serves, it is pointed out, as a highly potent calorigenic influence, particularly on the exposure of animals or man to low environmental temperatures.

The effects of medulli-adrenal secretion in reinforcing the heart and circulation, in the stimulation of glycogenolysis to provide increased blood sugar (fuel) for vigorous muscular contraction (thus augmenting body heat), and in the promotion of shivering movements, are emphasized in a paper corroborative of the foregoing[29], in which low body temperatures were studied. When small amounts of adrenalin were injected intravenously into animals in which artificial hibernation had been induced, they were found to stimulate reactions which tended to bring about a re-establishment of the normal body temperature.

Evidence is reviewed and reasons are also presented (Britton[29]) which lead to the belief that a natural autumnal diminution in activity of the highly differentiated adrenal tissues may result, in the case of comparatively (thermotactically) unstable hibernating organisms, in the commencement of winter sleep. Furthermore, the phenomena which are associated with the recovery of animals from hibernation—the rapid rise of body temperature, the remarkable increase in heart and respiratory rates, the augmentation of the blood-sugar level, vigorous shivering, and general stimulation of the arrectores pilorum—and also of artificially cooled homoiothermic animals from low body temperatures, significantly point to increased activity of the medulliadrenal mechanism as the immediate important agency in the thermal restoration process.

### DISCUSSION AND NOTES ON RECOVERY FROM EXPOSURE TO COLD

Considering the frequent occurrence of death from exposure to extreme cold in countries within the north temperate latitudes, it is important that the general and specific reactions to cold, as well as the particular condition of the organism at low temperatures, be more thoroughly understood. With this interest in view, an attempt has been made in the foregoing pages to evaluate the condition and effects of extreme hypothermia in man by the consideration and correlation of the various phenomena observed in lower animal types.

It is shown that the lowering of body temperature induces a progressive paralysis of the central nervous system. Consciousness disappears first, followed by the abolition of different reflexes as successively lower temperatures are reached. The effects of cold are, therefore, in many respects similar to those of anæsthesia.

Poikilothermic animals and certain hibernating forms maintain life even when their body temperature has been reduced to 0° C. or slightly lower. The hibernating woodchuck recovers spontaneously from a degree of cold that induces a deep rectal temperature of 3° C. True homoiothermic animals show on the other hand a distinct line of demarcation from other types, in that they may not be cooled beyond 16° C. without death supervening. From this critical body temperature for mammals, including some of the primates, artificial resuscitation to normal may be carried out. At the slightly higher body temperature of 19° C., perfect spontaneous recovery may be effected.

At very low body temperatures the homoiothermic animal, which may be considered as being most nearly allied to man, frequently appears on first examination to be quite lifeless. The cornea appears dull, and the pupil widely dilated and unresponsive to light and accommodation. The heart-beat and respiration may not be perceptible by ordinary methods, and noxious stimulation applied to any part of the body may elicit no response. The condition may be looked upon as one of extreme cold narcosis. The skin and subcutaneous tissues appear very cold and may be frozen, and an *ordinary* rectal or an anal thermometer reading may show a temperature almost approximating zero. It may be said that it is necessary, in order to obtain a true record of body temperature, that the thermometer be introduced either deeply into the œsophagus or to a depth of at least 8 cm. into the rectum. Such a *deep* body temperature will be found considerably higher than that elicited by an ordinary superficial placing of the thermometer.

Notwithstanding the foregoing as well as many other indications of the absence of life, it is to be emphasized that perfect restoration of such a severely cooled animal may commonly be effected. Vigilant scrutiny may be demanded in order to detect evidences of respiration, or of the heart-beat. An extremely slight vibration of the precordium may indicate the latter, even when the direct and stethoscopic methods have failed. Movements of the alæ nasæ are sometimes present, and indicate respiratory efforts.

One of the last reflexes to hold out against the paralyzing effects of cold is the knee-jerk. This reaction to patellar (mechanical) stimulation constitutes therefore a valuable sign of the persistence of life. It is to be noted that the reflex may be very slow in initiation and subsidence, even occupying two to four seconds in some cases. The reflex effect on respiration of dilatation of

the anal sphincter may also persist almost until death in cooling. On severe dilatation of the sphincter an asphyxial type of respiration is occasionally produced.

The presence of the more important bodily reactions in the mammal have been noted at various low temperatures as follows:—Knee-jerk, also micturition reflex, 16° C.; anal sphincter respiratory reflex, Achilles-thrust, 17°; stepping reflex, 18°; shivering, 19.5°; flexion reflex, phonation, 20°; corneal, sneezing and swallowing reflexes, 22°; pupillary reflex to light, 23°; equilibrium, sight, smell and hearing, 27.5°; co-ordinated action (walking, etc.), 28°.

Therapeutic doses of drug stimulants such as strychnine and alcohol have slow and relatively slight effects in severe hypothermia, probably because of the low metabolic rate of cooled animals.

The medulli-adrenal mechanism is shown to be specifically concerned in the chemical regulation of body temperature. The remarkable phenomena which are associated also with the awakening of animals from hibernation or from low body temperatures are strongly indicative of increased adrenal secretion. A very potent factor in organic thermogenesis, particularly in emergency situations such as may endanger life, is furnished by the markedly enhanced output from the adrenal glands.

Artificial respiration may usually be practised with success, even after spontaneous respiration has long since failed. Good results have been obtained with the tracheal tube introduced either *per os* or by tracheotomy. Warm baths or packs, gradually increased to higher temperatures within therapeutic limits, and also gastric lavage with warm fluids, are valuable aids to resuscitation.

A number of instances of the recovery of men from low body temperatures are quoted. A striking case on record is that of the resuscitation of an inebriate in whom the rectal temperature after exposure to cold registered only 24° C.

From the evidence herein adduced, showing the exceedingly low body temperatures (far below those observed in the human subject) from which the higher types of animals allied to man (in the thermotaxic sense) may fairly readily be resuscitated, it is indicated that man himself is *potentially* able to withstand much lower temperatures than have hitherto been recognized as compatible with life. It is therefore urged that such therapeutic measures for recovery as are briefly outlined above be immediately instituted in cases of apparent death from exposure to cold.

Considerable evidence has been adduced which indicates the marked calorigenic influence of adrenalin. The intravenous injection of small amounts of the substance has been shown to further remarkably the recovery process in extreme hypothermia. The effect may possibly result from the increased availability of glucose (as fuel) for the tissues, through the mobilization of glycogen from the liver by adrenalin. Injected glucose, indeed, appears to act similarly in accelerating recovery from cold.

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THE DANGEROUS EFFECTS OF WATER.—The dread of water can be traced back to a fairly remote period. In the first quarter of the sixteenth century bathing was considered a strange fad in England. The Grete Herball, printed by Peter Treveris in London, in 1526, gives Galen as the authority for the statement that "Many folke that hath bathed them in colde water have dyed or they came home." The drinking of water seems also to have been deemed harmful at that time and earlier. Prohibitionists will derive cold comfort from this statement, taken from the same herbal: "Mayster Isaac sayth that it is unpossyble for them that drynketh overmuche water in theyr youth to come to ye aege that god ordeyned them." Possibly, the rooted objection of the small boy to having his face washed may, after all, be natural, a sub-conscious "hang-over" from the past.—[ED.]

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# Men and Books

## BIBLICAL MEDICINE AND HYGIENE*

BY H. H. MURPHY, M.D.,

*Kamloops, B.C.*

"The past enthralls us because it is made up, not as professors fancy, of much that is buried, but of everything that lived."

"Honour a physician according to thy need of him with the honour due unto him: for verily the Lord hath created him. For from the Most High cometh healing: and from the King shall he receive a gift. The skill of a physician shall lift up his head: and in the sight of great men he shall be admired. The Lord created medicines out of the earth: and a prudent man will have no disgust at them."

So wrote Jesus, the son of Sirach, in *Ecclesiasticus*. These verses have received scant notice. One writer—a humourist, no doubt—correlates them, as is the theological custom, with certain New Testament verses, and concludes that these are the physicians of whom the woman with the issue of blood had suffered many things, and on whom she had spent all her living. Yet the proverbs of the ancient Hebrews refer to the physician in equally favourable terms: "A wise man will not live in a town where there is no physician"; "They that are whole need not a physician, but they that are sick"; "He that sinneth before his Maker, let him fall into the hands of the physician."

It has repeatedly been observed that the Hebrew race, in spite of centuries of wandering, is remarkably healthy. To-day it enjoys a relative immunity from tuberculosis (Osler), and when it does not lapse from the Levitical code, frequently escapes zymotic disease during an epidemic. This cannot all be attributed to the original vitality of the clan, because no Jewish blood is pure to-day. An explanation can be found, however, when we consider that what Israel Zangwill has termed the "pot and pan part of their religion" was, in reality, a religion of cleanliness, and implied the ability on the part of the priests to diagnose many diseases, and embodied rudiments of preventive medicine.

The connection between religion and medicine was, however, not an unmitigated blessing. Accurate medical knowledge, now obtained by post-mortem examination, was impossible, on account of the ceremonial uncleanliness which followed contact with a corpse. Further, the annual gathering of the people in high places aided in the dissemination of disease and was productive of much vice and immorality.

Two theories of the etiology of disease in general held sway: (1) the demonic—that some diseases were due to the possession of the patient by some demon, or, if the illness was very severe by a legion, at least, of evil spirits; (2) the punitive—that diseases were meted out as punishment by Yahweh for sins either of the patient or of some of his ancestors. Hence, when any one took sick, the head of the family carried an offering to some temple and asked as to the fate of the patient. If the answer came back that he must die, then, as with the Greeks, it was considered useless "to strive against the Gods." A favourable answer and the promise of recovery also freed the friends from anxiety and made treatment unnecessary.

While tracing their diseases, as they did their origin and theology, back to the "First Cause", the Jews recognized secondary causes as operative in the production of disease. When the Philistines were stricken with what was probably the bubonic plague they evidently recognized, as we do to-day, that the disease was carried from one section of the country to another by rats and mice, for they endeavoured to propitiate Yahweh by offering five golden images of the most noticeable result of the disease and five golden mice—images of the probable disseminators of the plague. Again, when the wanderers in the wilderness wearied of manna and craved for a more varied menu, an epidemic broke out in the camp, which the people attributed to the quail which they had just eaten (Numbers XI, 33). To-day we know that the quail probably carried infection to the Hebrew camp from some other band of wanderers, it may have been from some Bedouin caravan.

We are very proud to-day of our Social Hygiene Council and the work they are accomplishing, but let us not fail to recall the social hygiene injunctions of the Old Testament. These commands covered the prophylaxis and suppression of epidemics, the treatment of venereal disease, the checking of prostitution, the care of the skin, baths, food, hours of labour, and sexual relations. So conscious were the Jews that these laws were good that we find in Deuteronomy IV, 6, this added admonition. "For this is your wisdom and your understanding in the sight of the nations."

Nay more, we value to-day the work being done by our various Workmen's Compensation Boards in Canada, and we feel that they are entitled to the credit they claim of having been

* Read at the Annual Meeting, Canadian Medical Association, Section of Historical Medicine, June 21, 1929.

able to devise new safeguards in protection from machinery, so that accidents are less numerous. If you will refer to Deuteronomy XXII, 8, you will find a like safeguarding of workmen against possible accident.

"When thou buildest a new house then thou shalt make a battlement for thy roof that thou bring not blood upon thine house if any man fall from thence."

In Leviticus XI, verses 4, 6, 7 and 8, we find an interesting prohibition regarding certain clean and unclean animals. "Nevertheless these ye shall not eat of them that chew the cud, or of them that divide the hoof: as the camel, because he cheweth the cud, but divideth not the hoof, he is unclean to you. . . ." "And the hare, because he cheweth the cud, but divideth not the hoof, he is unclean unto you." "And the swine, though he divide the hoof, and be cloven footed, yet he cheweth not the cud; he is unclean unto you." "Of their flesh shall ye not eat and their carcasses shall ye not touch."

We have for years recognized that the Hebrew prohibited pork long before the dangers of tapeworm, trichina and hydatid had been associated with the pig, but until recently we paid little attention to the fact that the Hebrew could not eat hare, nor handle its carcass. Since Dr. George McCoy, of the United States Health Department Service, discovered the germ of rabbit plague and named it *B. tularense,* after Tulare County, California, and made possible the recognition of the first case in man by Dr. Vail in 1914, we realize that the Hebrew of Biblical days may have been a shrewd medical observer. Palestine was a semi-arid country and the results of eating hare or handling its carcass may have resulted in this prohibition, for we know to-day that handling the carcass of infected animals may be as dangerous as eating the meat.

From the accuracy of the Biblical descriptions we know that many diseases were recognized by the ancient Hebrews. Saul, "naturally a shy, self-conscious man, easily exalted into ecstacy and tyrannical self-satisfaction, possessed of an impulse to homicide, turning against his own son, and finally becoming despondent and meeting with death by suicide" (Hasting's *Bible Dictionary*), was a victim of recurrent paroxysmal mania. Nebuchadnezzar, like the daughters of Proetus, suffered for seven years from monomania, believing that he was a beast. Nabal, after a hearty supper and a somewhat riotous night, was stricken with apoplexy and died ten days later, or, as the Hebrew states it, "His heart died within him and he became as a stone, and it came to pass about ten days later that the Lord smote Nabal that he died." (1 Samuel, XXV, 37, 38).

Ahijah's eyes were "fixed by age," a poetic description of senile cataract. Epileptics were common in Bible days, as now, but nowhere do we find a more accurate account of an epileptic seizure than in St. Luke IX, 39: "And, lo, a spirit taketh him, and he suddenly crieth out; and it teareth him that he foameth again, and bruising him hardly departeth from him." Again, a priest who had contracted spinal caries could not minister in the sanctuary, and the same prohibition was applied to a man with a flat nose—doubtless a sign of the same disease that Hogarth meant it to be in so many of his pictures.

Palsy, of which we read so frequently, was equivalent to the word paralysis of to-day, a symptom of many diseases of the nervous system. The centurion's servant probably had meningitis (St. Matthew, VIII, 6), while the man with the withered hand (St. Matthew XII, 10-13) could probably date his disability from an attack of infantile paralysis.

Palestine was naturally a healthy land. A country of hills and valleys, with rapid streams not easily polluted, and having no harbours, could have few imported epidemics. Yet we read of diseases which we must attribute to the climate. One of the promises held out to the godly by the Psalmist was, "The sun shall not smite thee by day nor the moon by night," (Psalms, CXXI, 6), an immunity which would be valued by a community whose history recorded deaths by sunstroke, such as that of the Shunammite's son (2 Kings IV, 19), and of Menasses (Judith VIII, 3). In Deuteronomy XXVIII, 22, we have reference to fevers, probably of malarial origin, and to "consumption," which some have identified as modern pulmonary phthisis; while the Jewish proverb, that it is easier to rear a forest of olive trees than one child, would indicate that infantile diseases were exceptionally severe.

Surgical cases then, as now, were considered more dangerous and, consequently, brought greater fame to the successful physician. The woman bound by the spirit of her infirmity (St. Luke XIII, 11-17), was a case of senile kyphosis; while Lazarus (St. Luke XVI, 20), was the typical beggar outcast from society, who can be seen at any of our city dispensaries suffering from varicose ulceration. That the priests possessed some accurate surgical knowledge cannot be disputed, for the rite of circumcision was delayed if the child was jaundiced, a fact that would indicate that they appreciated the danger of hæmorrhage in such conditions.

Few cases of accident are described in the Bible, but that which happened to Abimelech is described at sufficient length to give us ground for diagnosing fracture of the skull, the retention of consciousness showing the absence of compression.

"The reproach of Van Helmont, that "a bloody Moloch presides in the chairs of medicine" could not be brought against the Hebrew

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physicians as the sacredness of blood prohibited bleeding. In Proverbs XXX, 15, we have reference to the use of leeches.

The Hebrew materia medica consisted of balm of Gilead, myrrh, cinnamon, cassia, aloes, calamus, spikenard, camphor, and mandrake. Folklore medicine, as amongst primitive people, attributed healing virtues to saliva, and the first aid to the injured rendered by the good Samaritan, when he poured oil and wine into the sufferer's wounds, was certainly surgically orthodox. They were ignorant, however, of dietary laws, and we cannot but think that Hezekiah was in greater safety when Isaiah prescribed a fig poultice than his kinsman who enjoyed a diet of fig pudding.

Osler, in his "pessimistic therapeutic nihilism," as some of his truthful statements about medicine have been termed by the American writers, has stated that much of the humbuggery of the profession still lingers about mineral waters. But if, as theologians tell us, "never yet has any particular doctrine or mode stating truth held its own for any length of time in human history unless there was some genuine truth beneath it" then we must still count mineral waters of some therapeutic value, since the Hebrews believed in their efficiency, even as the Gentiles of to-day. The saline waters of the Jordan, the miraculous healing power of the pool of Siloam, and waters of Bethesda were well known to all devout Jews. And to-day their descendants still bathe in the pool of Bethesda for rheumatism and other disorders. They still believe that the waters are more efficacious when they are "troubled" that is, when the natural syphon under the cave overflows.

One factor which probably contributed in no small degree to the health of the Jewish people was their care in providing good water supplies, that of Jerusalem being particularly complete. The city was supplied by five conduits. One, supposed to have been constructed by Solomon, was thirteen and a half miles long, two feet deep, and one and a half feet wide, and conveyed water from Solomon's Pool to the Temple. Another conduit connected this with a reservoir twenty-eight miles away. This latter passed through two tunnels, one four miles and the other seventeen hundred feet in length, while between the two was a reservoir which served as a sedimentation tank. The water was distributed in Jerusalem by leaden pipes to fountains, cisterns, and pools open to the public. We speak of the Jews as a primitive people, and yet contrast this water supply with that of many of our large cities—drawn from rivers of commerce within a short distance of polluted harbours, conducted to the city and stored in uncovered reservoirs, open to infection, to be distributed to a typhoid-stricken public without filtration or even sedimentation.

Of sanitation, as we understand the term to-day, the Jews knew little. The hungry dogs of the city acted as scavengers, and the sewage disposal was of the crudest character. But even as their primitive views of Yahweh as the national God evolved into the "one God, one law, one element," of to-day, even so were their ceremonial ordinances concerning leprosy the beginning of modern preventive medicine. Suspected lepers notified the priest; they were isolated for twenty-one days, and examined by the priest at weekly intervals. To-day we know that the Jews confounded many skin-diseases, such as vitiligo, with leprosy, but yet we see here the origin of our system of notification and quarantine of infectious diseases.

As regards food, the Jews were very particular, for was it not written in the law what a man should and should not eat? Animals of the herbivorous and ruminant groups were allowed, but no beasts of prey, nor could the fat or blood of any animal be used. In butchering there was, as there is at present, rigid inspection by one of the rabbis, who had definite rules for the detection of diseased meat. "Seven days shalt there be no leaven found in your houses:" (Exodus XII, 19), provided for a very necessary renewal of food supplies.

Amongst a people whose religious nature was so dominant such sanitary regulations could not but markedly effect the vitality of the race. For whether we regard them as the ear-marks of a people chosen by God, or consider them only in the light of their modern practical and hygienic value, the old promise is still true: "If thou wilt diligently hearken to the voice of the Lord thy God, and wilt do that which is right in his sight, and wilt give ear to his commandments, and keep all his statutes, I will put none of those diseases upon thee which I have brought upon the Egyptians: for I am the Lord that healeth thee." (Exodus XV, 26).

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POISONING BY ASPIRIN.—At the Sussex Assizes on July 9th a woman, aged 25, charged with poisoning her infant by means of aspirin, was found guilty but insane, and the judge directed that she be kept in custody as a criminal lunatic until His Majesty's pleasure be known. It appeared in evidence that the accused had dissolved 300 tablets of aspirin, each of 5 grains, in a pint of water, and, having given two dessertspoonfuls to the infant, had taken the rest herself; the infant died the following day. Dr. E. J. Budd-Budd stated that for a child two dessertspoonfuls of a solution containing 1,500 grains of aspirin to the pint would be a fatal dose. The defence was that the accused was insane at the time she committed the act.—*Brit. M. J.* **2**: 128, 1929.

# Association Notes

## BRITISH MEDICAL ASSOCIATION, WINNIPEG, AUGUST, 1930

THE arrangements for the meeting of the British and Canadian Medical Associations in Winnipeg next August are proceeding steadily and satisfactorily. About the middle of January Dr. T. C. Routley, the General Secretary, and Dr. G. Harvey Agnew, the Associate Secretary of the Canadian Medical Association, were in Winnipeg conferring with the local executive.

Some few corrections in and additions to the list of Officers of Sections, as it appeared in our December issue (p. 730), are to be noted. A new Section of Orthopædics has been instituted, of which the following are the officers:—

**President:**

E. Laming Evans, C.B.E., M.D., F.R.C.S., 50 Seymour St., London, W.I.

**Vice-Presidents:**

W. G. Turner, M.D., 900 Sherbrooke St., W., Montreal.
H. P. H. Galloway, M.D., F.A.C.S., Winnipeg.

**Honorary Secretary:**

A. P. MacKinnon, M.D., Winnipeg.

The following are the changes to be made up to the present, and it is possible that others will follow.

In the Section of Surgery the name of J. S. McEachern, M.D., is added to the list of Vice-Presidents. Also, C. W. Burns, M.D., 212 Medical Arts Building, Winnipeg, replaces Dr. A. P. MacKinnon as one of the Honorary Secretaries.

In the Section of Bacteriology, Pathology, Physiology, and Biochemistry, the Honorary Secretary for England is Professor Geoffrey Hadfield, M.D., M.R.C.P., Pathological Department, Royal Free Hospital, Gray's Inn Road, London, W.C. 1.

In the Section of Mental Diseases and Neurology C. C. Warster-Drought, M.D., M.R.C.P., 19 Cavendish Square, London, W. 1, replaces Dr. Macalpine as Honorary Secretary for England.

In the Section of Ophthalmology G. H. Whiteside Robertson, O.B.E., M.D., C.M., The Laurels, Caudie, Guernsey, is appointed one of the Honorary Secretaries.

In the Section of Preventive Medicine T. Eustace Hill, M.B., C.M., Durham, and W. G. Willoughby, M.D., D.P.H., Eastbourne (President-Elect, 1931), are appointed Vice-Presidents, and C. T. Maitland, M.D., M.R.C.P., D.P.H., 11 Beechcroft Avenue, Golders Green, London, N.W. 11, an Honorary Secretary.

In the Section of Radiology, Malcolm Donaldson, M.B., F.R.C.S., London, and J. Eugène Panneton, Montreal, replace Dr. J. M. W. Morison and Dr. Leo Pariseau, respectively.

In the Section of Medical Sociology and History of Medicine the names of John Smith Purdy, M.D., Sydney, N.S.W., and J. H. Harvey Pirie, M.D., F.R.C.P., Johannesburg, S. Africa, have been added to the list of Vice-Presidents, and of John D. Ewart, M.B., "Silverburn," Charlestown Road, Blackley, Manchester, to that of the Honorary Secretaries.

In the Section of Anæsthesia H. W. Weatherstone, M.D., Birmingham, and J. W. Magill, M.B., B.Ch., London, are appointed Vice-Presidents for England.

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## TENTATIVE PROGRAM

The following program has been arranged tentatively:

**Monday, August 25th:**

Registration at the Winter Club. Meeting of the Council, Canadian Medical Association, at the Royal Alexandra Hotel. Annual Meetings, M.M.A. and S.M.A. Boating and Tea at Kenora and Minaki.

**Tuesday:**

Registration at the Winter Club; Opening of the Exhibits by the President; Addresses of Welcome; Annual General Meeting; Reception of Delegates; President's Address. In the afternoon, the Cenotaph Ceremony in The Mall; The Religious Service (in the open air) at the Parliament Buildings; in the evening, President's Dinner (for Manitoba Club-men only); President's Reception at the Parliament Buildings (9 p.m.).

**Wednesday:**

Section Meetings (at the Winter Club and Court Houses). In the afternoon, Irish Graduates Luncheon; A Clinical Address at the Winter Club; Excursion to Lower Fort Garry. In the evening, a Public Meeting (Walker Theatre); Dance, and possibly a Reception at the Royal Alexandra Hotel.

**Thursday:**

National Temperance League Breakfast; Section Meetings. In the afternoon, Sectional Lunches; Alumni Classes; Golf; Two Clinical Addresses; Conferment of Degrees (Parliament Buildings); Private Garden Parties. In the evening, Annual Dinner; Public Meeting; Exhibitors' Smoking Concert; Dance.

**Friday:**

Medical Missionaries' Breakfast; Section Meetings. In the afternoon, Sectional Lunches; Alumni Classes; Golf; Two Clinical Addresses; Visit to Assiniboine Park. In the evening, Listerian Oration (Walker Theatre).

ROSS MITCHELL,
Chairman Publicity Committee.

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## WINNIPEG: ITS EARLY HISTORY AND INDUSTRIAL DEVELOPMENT

Winnipeg owes its situation to the junction of two rivers. In the post-glacial period Lake Agassiz covered what is now Manitoba as well as parts of Saskatchewan, Western Ontario, North Dakota, and Minnesota. Since the ice-belt at the north of the lake prevented the passage of the waters into Hudson Bay, the great basin spilled southward by the Red River Valley, and reached the Mississippi. The old beaches of Lake Agassiz are still plainly to be seen, and the finer deposits offshore make some of the flattest and most fertile prairies. The final separation of the ice sheets permitted the waters to flow northeast, but remnants of Lake Agassiz still remain to form Lake Winnipeg and other Manitoba lakes. The Red River, which in former days flowed southward, now flows northward into Lake Winnipeg, which in turn drains by the Nelson River into Hudson Bay. The Assiniboine River, rising in Saskatchewan, flows eastward and joins the Red River forty miles above Lake Winnipeg. With these points in mind the reader will appreciate the topography of the country about Winnipeg, and the meanderings of the two rivers.

So far as is known, the first white man to reach the spot where Winnipeg now stands was La Vérendrye, a native of Three Rivers, Quebec, who saw service in America and Newfoundland, and fought at the battle of Malplaquet, where, with nine wounds, he was left for dead on the field. Still seeking adventure in the peace that followed, he returned to Canada, and in 1738 voyaged by water from Montreal to discover a route to the Western Seas and to open up, for France, trade with the Indians of the plains. Travelling up the Red River from Lake Winnipeg, he reached the Assiniboine and passed up the latter to establish Fort La Reine near the present town of Portage la Prairie. He was shortly joined there by De Lamarque, one of the party, who had meanwhile built at the confluence of the rivers a small post called Fort Rouge. A suburb of Winnipeg still bears this name.

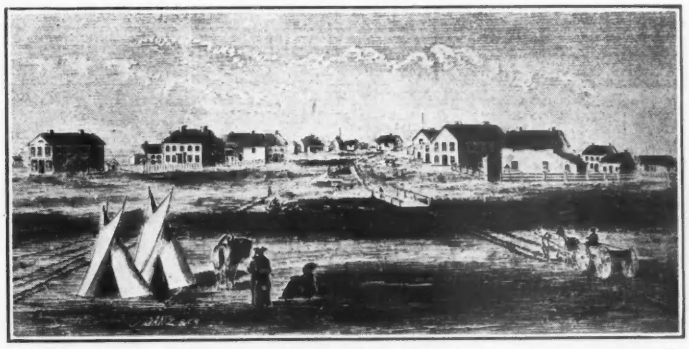
Some years after the British conquered Canada the North-West Company of Montreal pushed forward from their post at Fort William on Lake Superior, and, passing over La Vérendrye's route, established several trading posts from about

1780 onwards. In 1807 one of these, called Fort Gibraltar, was erected at the junction of the Red and the Assiniboine rivers.

Following the year 1800, "the Governor and Company of Adventurers of England trading into Hudson's Bay," who had for over a century been extending their huge dominion from the Bay, established posts on the Red and Assiniboine Rivers. In 1811 this company conceded to the Earl of Selkirk the privilege of placing a colony on the Red River, granting him for this purpose some 116,000 square miles of the surrounding country. The first of these settlers sailed from Stornoway, Scotland, in 1811, and wintered at York Factory on Hudson Bay, continuing a journey of much suffering and hardship to reach their destination in 1812.

For years there had been bitter trade opposition and personal animus between the men of the North-West Company and those of the Hudson Bay Company. The advent of the Selkirk settlers intensified this feeling, and the North-West Company made it known that they intended driving the settlers out, since land settlement was detrimental to fur trading. The culmination of the feud was the tragedy of Seven Oaks, when Governor Semple of the Hudson Bay Company and a score of Selkirk settlers were killed. A monument marks this spot.

In 1821 the two great companies amalgamated under the title of the Hudson Bay Company. The next year Fort Gibraltar, which had been destroyed, was rebuilt and christened Fort Garry. It stood until 1882, when it was pulled down, with the exception of the north gateway, which has been preserved in a small park. In 1831 the company commenced building Lower Fort Garry, twenty miles further down the Red River. This stone fort, with its buildings, wall, bastions, and many interesting relics, happily has been preserved, and forms a link with the past.



**Red River Settlement, 1868, which grew into the City of Winnipeg**
(Courtesy of J. H. Ashdown Co.)

In 1869-70 occurred the first Riel rebellion. The French half-breeds, protesting against the surrender of the rights of the Hudson Bay Company involved in Canadian confederation, formed a provisional government. Riel seized Upper Fort Garry and terrorized the people of the district until forced to fly to the United States by the arrival of the Wolseley expedition. This force consisted of the 60th Rifles and other English Regulars, together with Canadian Militia from Eastern Canada. The troops were quartered for some time in the Lower Fort.

Nor was this the first time that English troops had been in the Fort Garry settlement, for in 1846 Colonel Crofton, with some 400 men, including a wing of the 6th Foot and detachments of artillery and Royal Engineers, had been dispatched at the request of the Hudson Bay Company, owing to the threat of war between Great Britain and the United States over the Oregon boundary question. The force remained for a year, and following this some British pensioners were sent out, many of whom remained in the country.

The village of Fort Garry was incorporated as the City of Winnipeg in 1873, and since then its growth has been steady, accelerated in 1883 by the arrival of the main line of the Canadian Pacific Railway, gradually followed by other lines, including the Canadian National Transcontinental. The earlier settlers came from Ontario, while later settlers came from the British Isles, the United States, and European countries.

For a quarter of a century Winnipeg metaphorically carried its eggs in one basket. The basic industry of the Canadian West was agriculture, and with the success or failure of the crops the city's prosperity rose and fell. In recent years, however, the yield of the soil has ceased to be all-important. The development of hydro-electric power, the discovery of minerals in the northern part of Manitoba, and the completion of the long-discussed railway line to Hudson Bay have directed activities into new channels.

Winnipeg is naturally the hub of all industrial activity for the province, and by the way it has gone ahead in the last five years it reflects the general progress made by Manitoba as a whole. Material contributory factors have been the great development of hydro-electric power; mining activity, which includes investment of tens of millions of dollars, particularly in the north country; railway expansion, giving access to new territory and fresh resources; increase in industrial development with mounting pay rolls; and greater returns from agriculture through diversification in farming.

Winnipeg is also the centre of the grain trade of the whole country, as well as of many of the allied industries which have developed. Here are located the great selling agencies of the West's grain crop, the Wheat Pool, and the Winnipeg Grain Exchange, which divide the handling about

equally between them. It is the seat of the Canada Grain Commission, which is responsible to the Dominion Government for the administration and interpretation of the Canada Grain Act. The bulk of the grain is inspected at this point for grade standards in the largest and most important plant of the kind in the world. And from this centre the transportation departments of the two great railway systems direct the gigantic task of moving the crop each year.

Brief comment on the leading activities of Manitoba and its capital city may not be without interest. The only commodity it paid the earliest settlers to "pack out" was fur, and it was not until after 1870 that wheat began to be thought of as an export. Indeed, the very fertility of the soil was seriously questioned up to that time except along the silt-enriched banks of rivers. Neither was the fluidity of grain recognized, and men transported the early crops in jute bags. Other methods of handling were equally laborious.

**Primitive Transport—A Red River Ox Cart, from an actual photograph**
(Courtesy of J. H. Ashdown Co.)

The advent of the railroad made export both possible and profitable, and rapidly mounting growth in production was met by the gradual evolution of the most complete bulk handling system, participated in by the banks, the transportation companies (rail and navigation), the Government, and the grain trade. Proper handling has meant the provision of enormous storage capacity, with facilities for weighing, scouring, cleaning, drying, special binning, and efficient loading. It has meant the training of thousands of persons for the diverse phases of handling from the time the grain leaves the farmer's wagon-box until it passes out of the country. The heart of all this activity is Winnipeg.

Wheat production in 1928 reached the high mark of considerably more than half a billion bushels, and elevator storage capacity stood at nearly half that figure, including harbour front terminals as well as the interior elevators into which the farmer weighs. The Wheat Pool last year erected a handsome new headquarters for its central selling agency at Winnipeg. In 1928 the Winnipeg Grain Exchange thrust out a new half-million-dollar wing, and is again cramped for trading space. It is the largest cash grain market in the world where the greater part of the trading is backed up by the actual grain. The bulk of the 1928 export of grain—almost half of what the whole world consumed—was handled through Winnipeg.

The story of persistent research and experimentation in connection with the evolving of an all-round suitable kind of grain is a romance in itself, which can barely be touched upon. Some years ago three heads of wheat were saved by an Ontario farmer, out of a sample of seed grain sent him from Scotland, and since traced to the Ukraine. These three heads became the ancestors of "Red Fife," which in turn, bred and crossed with Russian and other hardy northern varieties, brought forth "Marquis" wheat, the present standard. "Marquis," whilst of excellent milling quality, early maturing, and frost-resistant, is not "rust" proof, and so a fresh intensive research is going on at the present time in the Government Rust Research Bureau, located at Manitoba Agricultural College, for a variety which shall retain all the good qualities of "Marquis" and be rust-resistant as well. Success in this instance will mean a saving of untold millions to the country.

The rapid increase in industrial production in Manitoba, which last year surpassed agricultural production by 10,000,000 dollars, is due in the main to one great economic factor—the development of plentiful and cheap hydro-electric power. Besides the benefits accruing to the city from the added pay rolls, it has become the first electrical city of the world, with an average of 3,384 kilowatt hours' annual consumption per residence. The cost is the lowest on record—a shade above three-quarters of a cent per kilowatt hour, as against an average cost of 7.16 cents in 172 representative American cities. Towns and villages throughout the province are rapidly being supplied with power, and the erection of transmission lines is keeping pace with the harnessing of waterfalls. Pulp and paper mills are included among the industrial enterprises which have followed in the wake of power production.

The total resources of the province in hydro-electric power are placed at 5,000,000 horse power, of which 3,000,000 are on the Nelson River, convenient to the mining belt of the north, and 800,000 on the Winnipeg River, within easy transmission of Winnipeg. The total development, so far, consists of three sites on the Winnipeg River, producing 308,000 horse power. Two

other sites on the same river—Slave Falls with 90,000 horse power and Seven Sisters Falls with 225,000 horse power—are being developed, as well as one 50,000 horse-power hydro-electric plant in the northern mining area.

The full story of how the first of the equipment and machinery for the development of hydro-electric power was "packed" into the wilderness on the backs of men, of the overcoming of swamps and morasses, of mosquito-infested trails, of the excavating of thousands of tons of rock, and of the damming of lakes and rivers, may never be told as it deserves. But one thing is certain, and that is that the great waterfalls, beside which the toilers of an earlier era sometimes dropped dead under their 200-pound load per man during the portages, from now on will not be called "majestic and frightful," as Daniel Harmon said of them in his famous journal in 1800, but "majestic and useful."

The presence of valuable copper deposits along the Coppermine River on the Arctic border, has been known since the discoveries of Samuel Hearne in 1771-72, but they are still inaccessible. Similarly, the buffalo hunters who rode the trails on the great hunts in the fifties and sixties, knew of the lignite deposits in the Souris Valley on the south-western Manitoba border, but it was not until the railroad came that the knowledge could be put to general use. Something less than one-fifth of the surface of this province is arable, leaving an immense area in which it was possible to prospect for minerals, metallic and non-metallic, and yet it is a bare eighteen years since the beginning of Manitoba's metal-mining development, although production of non-metallics commenced earlier.

The returns from metallics have not been large so far, and will not be until the great plants, now being erected at enormous cost in the hinterlands of the province, bring the properties they are designed to serve into production. The largest of these are the Flin Flon and the Sherritt Gordon properties north of The Pas near the Saskatchewan border. The Hudson Bay railway cutting through this region is now an accomplished fact after more than forty years of "talk," and branch lines from it connect with both these properties. The Island Falls power site, ninety miles distant, now under development, will furnish the needful power.

When the Flin Flon mine is brought into production 3,000 tons of ore will be treated daily, with an approximate annual production of 30,000,000 pounds of copper and 50,000,000 pounds of zinc, as well as values in gold and silver, according to information supplied by the industrial development department of the Canadian Pacific Railway. A concentrator and smelter is now being erected to treat these ores. The Sherritt Gordon property, which is a near neighbour, will have a higher yield per ton, and contains copper-zinc ore with values in gold and silver also. A 1,500-ton concentrator is under construction on the property, while the copper concentrates will be smelted at the Flin Flon smelter. The "Mandy" is another property in the same area from which considerable high-grade ore was taken in 1917-19, with diamond drilling under way at present for the location of further ore bodies.

In the southern Manitoba mining field the Central Manitoba Mines is the only producing concern at present. A 150-ton mill has been in operation here since 1927, and gold to the value of 770,483 dollars was shipped to the mint at Ottawa last September. Hydro-electric power from Great Falls on the Winnipeg River supplies this plant. Other mines in this area, where developmental work is now taking place, are the San Antonio and the Gem Lake. Minerals, other than those named above, which have been discovered in the province are tin, silver, arsenic, cobalt, iron, lead, nickel, molybdenite, tungsten, and beryllium.

For some time past the province has had a very real asset in the non-metallic minerals, which have been responsible for more than 75 per cent of the mineral production to date. Of these, the group of structural and building material is the most important. First in rank is building stone (Tyndall stone), which is a limestone quarried thirty miles east of Winnipeg, and of so high a quality that it is being shipped to all parts of Canada. It is seen in Manitoba's public buildings and many of its business houses. The brick and tile industry is also important; gypsum has been produced for a number of years; and sand, suitable for glass manufacturing and moulding, is also available in large quantities.

A discovery which may be of considerable importance commercially is that of large quantities of lithium ore along the Winnipeg River, near the Ontario boundary. Considerable development of this find has already taken place, and ore has been shipped to Europe for extracting the lithium. The discovery has brought Manitoba conspicuously before other parts of the world in view of the fact that here is one of the largest sources of supply of a non-metallic mineral whose uses are rapidly increasing. Other non-metallics found in the province are limestone, granite, marble, bentonite, feldspar, garnet, salt, peat, coal, oil, and gas. There has, however, been very little production of any of the latter named.

A great deal of prospecting is now taking place, and it would not be surprising if new discoveries of first importance were made within the next few years, more especially in the non-metallic minerals in the northern part of the province — *Brit. M. J.* **1**: 31, January 4, 1930.

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## LEADERS IN BRITISH MEDICINE

Not the least delightful feature of the forthcoming meeting of the British Medical Association in Winnipeg next August will be the presence of many distinguished visitors, men whose names are household words in the old land, and whose fame as scientists has become international. Some of them have been in Canada before; others are visiting it for the first time; all will be welcome. It is hard to over-estimate the stimulus that will come to the Canadian profession from contact with these outstanding personalities. It will not be amiss to give in the pages of our *Journal* a few biographical notes about some and in particular those who are to serve at the head of the various Sections.

### RT. HON. LORD DAWSON OF PENN

Sir Bertrand Dawson, K.C.B., K.C.M.G., G.C.V.O., B.Sc., M.D., F.R.C.P., the Right Honourable Lord Dawson of Penn, who is the President of the Section of Medicine, is the son of a distinguished architect, Henry Dawson, F.R.I.B.A., and was educated at University College and the London Hospital. He received his M.D. degree in 1893, and became Assistant Physician to the London Hospital in 1896, and Physician in 1906. He is also Consulting Physician to the King Edward Seventh Sanatorium and the Royal National Hospital for Consumption at Ventnor; member of the Senate of the University of London; and President of the Royal Society of Medicine. At first Physician-Extraordinary to King Edward Seventh and to His present Majesty, he was created Physician-in-Ordinary to King George in 1907 and the Prince of Wales in 1923. He was created Baron Dawson of Penn in 1920.

In 1890 he married the youngest daughter of Sir Alfred Yarrow, head of the great Clyde shipbuilding firm. He has three daughters. Lady Dawson has received the Order of the British Empire.

Lord Dawson has contributed many articles to Allchin's Manual of Medicine, and has written largely on general medical topics.

### RT. HON. LORD MOYNIHAN OF LEEDS

Sir Berkeley George Andrew Moynihan, created K.C.M.G., in 1912, Baronet in 1922, and Baron in 1929, was born at Malta, the son of Captain Moynihan, V.C., 8th (King's) Regiment, and educated at the Royal Naval School. He holds the following qualifications: M.S., M.B., F.R.C.S., F.R.C.S.I. (hon.), F.A.C.S. (hon.), besides degrees from the Universities of Leeds, Edinburgh, Bristol, Ghent, Dublin, Belfast. He is President of the Royal College of Surgeons; Honourary Surgeon, Leeds General Infirmary; Professor of Clinical Surgery, University of Leeds. He is a recognized authority on abdominal surgery, particularly that relating to the biliary passages. He has also written on the spleen and pancreas. Lord Moynihan served in the R.A.M.C. during the Great War, being mentioned in dispatches. He retired with the rank of Major-General.

In 1895 Lord Moynihan married Isabella Wellesley, daughter of T. R. Jessop, F.R.C.S., and has one son and two daughters. Lord Moynihan is not only a commanding figure in every way but a speaker of rare eloquence and power.

Lord Moynihan will act as President of the Section of Surgery, and is also Listerian Orator.

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## THE CANADIAN MEDICAL ASSOCIATION

The Executive Committee of the Association met in the Chateau Laurier Hotel, Ottawa, on Tuesday, November 19, 1929, commencing at ten o'clock in the morning and continuing throughout the day and evening. Thirteen members of the Committee were present, out of fifteen.

Many important matters affecting the welfare of the medical profession came up for discussion, among which were the following:—

### HEALTH INSURANCE

It was reported that, in British Columbia, a Commission of five members of the Legislature (two of whom are doctors) has been appointed to study the problem of Health Insurance as it affects that province. Attention was also called to the fact that the Department of Pensions and National Health, Ottawa, has under consideration the making of a study of this matter in its relation to all Canada. The Canadian Medical Association has been securing copies of literature bearing on this subject, not only from the different provinces of Canada but from other countries. At the request of the Executive Committee, the Secretary of the Department of Publicity and Health Education is now engaged in making a summary of this material, in order that it may be available for the information of our members.

### DEPARTMENT OF HEALTH EDUCATION

The following report was made to the Executive Commitee with reference to the work of the Department of Publicity and Health Education:—

| | |
|---|---|
| Number of newspapers receiving health articles released on Wednesdays .... | 175 |
| Number of newspapers receiving health articles released on Saturdays .... | 155 |

Total number of newspapers using this service ..... 330
Total circulation of newspapers using the service ..... 1,865,040

This particular department of our work is being financed by means of a grant of $6,000 from the Canadian Life Insurance Officers Association.

Commencing with January 1, 1930, a special series of health articles will appear in Maclean's Magazine, under the auspices of the Canadian Medical Association. By this means, the circulation of our health service will be greatly increased.

In addition to publications in the press, steps are being taken to broadcast five minute health talks, once a week, through the Canadian National Radio Service, commencing early in the New Year.

### PERIODIC HEALTH EXAMINATIONS

The Executive Committee was advised that four insurance companies have already agreed to enter into the Periodic Health Examination plan of the Association, commencing on January 1, 1930, and that one additional company is seriously considering doing so. Dr. H. H. Murphy, formerly of Kamloops, B.C., will have charge of this new Department, and enters upon his duties in the Toronto office on January 2nd.

There has been such a demand for the moving picture film illustrating the conduction of a physical examination that the Executive Committee decided to procure two additional copies.

### B.M.A.–C.M.A. ANNUAL MEETING

Arrangements are well under way for the conjoint meeting of the British Medical Association and Canadian Medical Association to be held in Winnipeg during the week of August 26, 1930. According to present indications, there will be a record attendance at this meeting, not only from Canada and the British Isles, but from other more distant parts of the British Empire and the United States. This meeting will be an outstanding event in the history of medicine in Canada, never to be forgotten by those privileged to attend.

The headquarters of the meeting will be the new Winter Club, which offers excellent facilities for the many activities connected with the meeting.

It is the custom of the British Medical Association to have for distribution at each annual meeting a souvenir book called "The Book of the Meeting," descriptive of the particular city or locality in which the meeting is held. For the 1930 meeting, it has been decided to prepare "The Book of Canada." This is now under way, the editors being Professor Chester Martin and Professor Stewart Wallace of the Department of History of the University of Toronto. Ne effort is being spared to make this a volume to be admired and prized by our guests and members.

In the near future, important information will appear in the *Journal* in reference to transportation to Winnipeg. It is the desire of the Executive Committee that the best possible arrangement be secured for those travelling to the meeting.

As only members in good standing in the Association may attend the Winnipeg meeting, the Executive Committee instructed that members be urged to send in their fees for the year 1930 at an early date.

### PRIMARY F.R.C.S. EXAMINATION

A communication was presented to the Executive Committee from the Royal College of Surgeons of England, expressing their satisfaction with the results of the primary examination held in Toronto last August, and their willingness to hold the examination in Canada again next year, provided that a sufficient number of candidates make application. The Executive Committee was of the opinion that the next examination should be held in Montreal during the month of September.

### THE MARINERS COMMITTEE

The Chairman of the Mariners Committee forwarded to the Executive Committee the following recommendations which were approved by his Committee.

1. That existing hospital contracts dealing with the care of sick mariners be renewed on the basis of $2.50 per diem, such contracts to exclude medical and surgical services.
2. That remuneration for medical services be arranged directly with the doctor, on the basis of fee schedule or other satisfactory arrangement.

The above recommendations will be dealt with by Council at the annual meeting next August.

### LIBRARY FUND

The treasurer reported that Dr. A. D. Blackader, of Montreal, had very kindly donated the sum of $50.00 to the Department of Hospital Service, to be used towards the establishment of a library for the Department. Dr. Blackader has since that time made an additional donation of $60.00 towards the library fund. The members of the Committee expressed their hearty appreciation of the kindness and generosity of Dr. Blackader, this being only one of many occasions upon which he has exhibited in some tangible way his interest in, and keen desire for the success of the Association and its activities.

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### THE POST-GRADUATE DEPARTMENT

The Post-Graduate Department of the Association completed the fourth year of its operation on September 30, 1929. The following summary for the four years, as presented to the Executive Committee, will serve to indicate, to a certain extent, the scope of the work accomplished:— (See table below).

### STUDY COMMITTEE ON NURSING

The survey of nursing education, inaugurated by the Study Committee on Nursing of the Canadian Medical Association and Canadian Nurses' Association, is now well under way, under the direction of Professor Geo. M. Weir, of the University of British Columbia, who has been granted leave of absence by his university in order that he may carry out this important piece of work. This undertaking is being financed by the Canadian Nurses' Association, the Canadian Medical Association, and the Ontario Medical Association.

### NARCOTIC DRUG ADDICTS

Attention was called to the fact that, as the Narcotic Drug Act now stands, the drug addict comes under the criminal code. There is no provision made for his treatment except in an insane asylum. The recommendation was made that the Provincial Governments be requested to provide institutions for the proper treatment of these people, under the direction of doctors experienced in caring for such cases. This matter will come up for further consideration at a later date.

### GROUP MEMBERSHIP

A communication was brought to the attention of the Executive Committee inquiring as to whether reduced rates for membership in the Association could be secured where two or more doctors are in a group, and where only one copy of the *Journal* is necessary. It was pointed out that, as the *Journal* is but a perquisite of membership in the Association, and the fee for membership is $10.00, there could be no reduction of this amount; but the Executive Committee recommended that all doctors not requiring their journals pass them on to medical missionaries or others worthy of receiving them gratuitously. This action is now being taken by many doctors ,and is very much appreciated by the recipients.

### CONCLUSION

Many other matters of routine business engaged the attention of the Executive Committee, adjournment being made at 11.00 p.m., after an all-day session.

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## THE SURVEY OF NURSING EDUCATION

During the first two months of the Survey, the Director, Dr. George M. Weir, has been laying the foundation for the study of nursing in Canada. In addition to the preparation of ten special questionnaires, Dr. Weir has held conferences and interviews, has made visits to hospitals, has attended lectures, demonstrations, etc., for observation of methods of teaching student nurses and has given psychological examinations to 300 student nurses. Based on these examinations, a prognostic study has been made regarding leadership and possible success as a nurse.

A community study regarding the nursing needs of the family of average means has been organized in a general way. This study has been carried out in co-operation with the Social Service Department of the University of Toronto.

A study of the following is being organized,— curriculum, examination standard, the cost of nursing education and the educational and economic features of the centralized lecture plan.

More than one hundred letters have been returned to the Director's office, owing to faulty addresses of registered nurses supposed to be resident in Ontario. All nurses in Ontario who have not received a questionnaire inviting them to participate in the Survey should write the Director, 1 Queen's Park, Toronto 5, stating the branch of the profession to which they belong and a questionnaire will be forwarded at once.

It is necessary that all registered nurses should support the Survey by taking an active part if the results anticipated from the study of nursing education are to be realized. At a later date, opportunity will be given for nurses in the other provinces similarly to participate in this study. Results of the investigation throughout the Dominion will then be integrated and interpreted.

| | 1926 | 1927 | 1928 | 1929 | Totals |
|---|---|---|---|---|---|
| No. of Speakers ..... | 169 | 269 | 329 | 379 | 1,146 |
| No. of Addresses ..... | 513 | 729 | 802 | 730 | 2,774 |
| Average attendance per lecture ..... | 29 | 27 | 31.7 | 36 | |
| Total attendance ..... | 17,264 | 19,683 | 25,423 | 26,287 | 88,657 |
| Total cost ..... | $30,100.27 | $28,831.66 | $33,336.45 | $31,257.21 | $123,525.59 |
| Cost per lecture per doctor | $1.74 | $1.46 | $1.31 | $1.19 | $1.43 |

# Hospital Service Department Notes

## HOSPITAL SERVICE FOR PATIENTS OF MODERATE MEANS

This subject is considered in Publication Number Four of the Committee on the Cost of Medical Care which is now in the course of a five-year program of study of the economic aspects of the care and prevention of illness in the United States. Many of its observations may be of interest to the medical staffs of Canadian hospitals, especially as some Canadian hospitals are included in the tabulations.

There are definite indications that the patient of moderate means, with a small income but a desire for privacy, is receiving increasing attention. For instance, the long open public wards are being replaced by small wards, semi-private rooms, and cubicle arrangements. In 1908, 28 per cent of the beds of a certain group of new hospitals were in wards of ten beds or more capacity; in 1928, the percentage in a corresponding group was seven. Simultaneously, the proportion of beds in semi-private rooms increased over the twenty-year period from 10 per cent of the total number of beds in the hospitals designed in 1908 to 23 per cent in 1928. There is less distinction now between "ward" and "private" patients, between "steerage" and "first cabin" passengers. Now, there is a "cabin class" in the semi-private rooms and small wards. One-sixth of the hospitals reporting future plans are designing new construction which will be primarily for the use of patients of moderate means. The Massachusetts General Hospital is building a special 300-bed unit for the use of such patients.*

### Hospital Rates

The figures reported are interesting. Of 26,900 single rooms reported upon, one-fifth are priced under $5.00; two-fifths are $5.00 to $6.99; almost one-quarter, $7.00 to $8.99; and more than one-seventh, $9.00 to $15.00 and over.

*Extra or special service charges*; for operating room, anæsthesia, laboratory service, x-ray, special nurses, etc., have been studied, as these have been estimated to comprise from 30 to 60 per cent of the average hospital bill. A number of the hospitals participating in the study have inaugurated one of the following measures: *the graduation of special-service charges:* the partial elimination of these charges; or the placing of such charges upon a flat rate basis. *Inclusive charges* are being arranged by several hospitals, such arrangement being available for maternity service, tonsillectomies, and diagnostic service.

### Financial Adjustments

Owing to the unforseen financial demands of sickness, some form of financial adjustment seems necessary. A number of hospitals have instituted a *deferred or instalment basis of payment*, the schedule ranging over a period as long as three years. In a number of instances this plan has proved very successful; in others, even disastrous. The success of this policy of deferred payments "may depend upon the extent to which such a policy goes hand-in-hand with a careful preliminary investigation and a definite procedure for collections."

There seems to be a definite closer co-operation between the physician and the hospital in their financial relations with the patient. In some cases, doctors' fees are reduced to ward patients, either by informal understanding or explicit limitation. In a few instances, doctors' fees are collected by the hospital. "There is a slowly crystallizing recognition that the interests of hospital, physician and patient are best served where the patients' total financial outlay for his illness is considered as an economic unit."

The Committee points out that their study to date does not answer the vital question: "Would the patient of moderate means be able to pay for his hospital care even if the entire hospital world should adopt every one of the new policies outlined in this study? Can the patient of moderate means normally pay for his hospital bed, his "extras," his special nurse, and his physician, out of his own individual income? These hospital experiments will create a valuable fund of experience on this point but further studies must be undertaken of hospital, costs, distribution of wealth, and the possibilities of insurance.

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## THE HOSPITAL SURVEY IN ONTARIO

It appears that Ontario may soon see some definite revisions in its hospital legislation. The provisions and the interpretation of the present Hospital Act, especially in its definition of residency, have not been entirely satisfactory

*The new private wing of the Toronto General Hospital is also being especially designed and organized to meet the requirements of this type of patient.

**All communications intended for the Department of Hospital Service of the Canadian Medical Association should be addressed to Dr. Harvey Agnew, Secretary, 184 College Street, Toronto.**

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to the hospitals of Ontario, many of whose handicaps still remain for consideration.

To bring this Act up to date, and to study ways and means whereby the sick of this province may receive the best and most scientific hospital care, coupled with the most efficient and economical types of administration, the Ontario Government has appointed a Royal Commission on Public Welfare empowered to investigate hospital conditions from every angle. The three gentlemen chosen, Mr. P. D. Ross, of Ottawa; Mr. David M. Wright, of Stratford, and Mr. John M. McCutcheon, of Toronto, are all keen, broad-minded men, fully cognizant of the needs of the public, appreciative of the problems of the administrator and the physician, and are men who well realize the heavy responsibility of their task.

As outlined in the order-in-council, this Commission will study the organization, administration, inspection and supervision of public general hospitals, private hospitals, sanatoria, homes for incurables, public and private mental hospitals; penal and corrective institutions, including reformatories, industrial farms and gaols, orphanages, houses of refuge, infants' homes; agencies for the care of children, subnormal persons, aged persons, mothers in dependent circumstances; any cognate subjects or matters brought to their attention; methods employed in other provinces or other countries in dealing with any of the subjects or matters referred to the Commission; and the best methods of arranging for the control, inspection, co-operation and efficient economical management of these activities.

This Committee has assumed heavy obligations, indeed. Already numerous sessions have been held with representatives of the various organizations interested in the care and welfare of the sick. The Ontario Hospital Association, through its representatives, presented a strong case for various reforms long desired by the hospitals; such as, an increase in the government and municipal grants for indigents to equal the actual cost of care; the application of the government *per diem* grant to *all* patients, as in many other provinces; monetary assistance for the care of babies of indigent mothers; a more satisfactory definition of indigency; relief for hospitals and doctors caring for non-paying traffic accident cases; the subsidization of nurses' training schools as educational institutions, thus lowering the cost of hospitalization; provision for sailors, "drifters," and others without permanent home in Ontario; provision for narcotic addicts; the establishment of diagnostic centres; and other highly desirable revisions.

The Commissioners propose to visit a number of the hospitals and other institutions following the formal sittings. A final report from these gentlemen is not anticipated for some months, but it is said that an interim report may be available for the consideration of the legislature this coming session.

## CHEAP ANTI-FREEZE FOR FIRE PAILS

A number of rural hospitals wherein the high pressure water hydrant is *non est* depend for fire protection upon the fire-extinguisher and the time-honoured row of fire buckets. Where the latter are placed in outbuildings or poorly heated passage-ways there is some danger of freezing in cold weather, and in this condition they are of very little use for the purpose for which they were intended and for which seconds may prove beyond price.

To keep the water from freezing calcium chloride has been recommended. This has been used as an anti-freeze in motor car radiators but has not become very popular due to its action on the rubber tubing and upon soldered joints. A commercial grade of calcium chloride, containing water ($CaCl_2$—2 $H_2O$), and known as "75 per cent" calcium chloride is recommended, as this preparation is quite cheap. The following table, prepared for us by Mr. J. Stuart Wilson, biochemist, indicates the number of pounds of the calcium chloride required per gallon of water to depress the freezing point to various levels:

| *Lbs. 75 Per Cent $CaCl_2$ Per Gallon of Water* | *Freezing Point of Solution* |
|---|---|
| 1.5 | +18.0° F. |
| 1.8 | +12.0° F. |
| 2.2 | + 6.5° F. |
| 2.6 | - 2.0° F. |
| 3.0 | -12.5° F. |
| 3.4 | -23.5° F. |
| 3.75 | -36.5° F. |

If sodium chloride (NaCl) be used, the freezing point can be lowered by adding the following percentages of common salt:

| *Percentage of NaCl* | *Freezing Point of Solution* |
|---|---|
| 5 | +25.4° F. |
| 10 | +18.6° F. |
| 15 | +12.2° F. |
| 20 | + 6.9° F. |
| 25 | + 1.0° F. |

Another point may be of interest. A pail, even though painted red and distinctly labelled "For Fire Only," so frequently proves handy for other purposes that more than one fire has obtained good headway while a search was conducted for the roving buckets. To overcome this tendency, fire-pails may be obtained with convex bottoms, rendering them useless as containers unless held in the hand or placed upon a special rack.

### ALCOHOL FOR HOSPITAL USE IN BRITISH COLUMBIA

The hospitals of British Columbia have recently protested against a ruling of the Liquor Control Board which is far from fair to the hospitals and is a contributing factor to the cost of hospitalization.

Early in 1929 the hospitals of the Province of British Columbia were notified by the Liquor Control Board that in future ethyl alcohol must be purchased through the government liquor stores instead of directly from the distilleries. The hospitals, previous to this order, were securing their alcohol directly from the distilleries at a price of $2.50 per imperial gallon, plus $14.85 excise tax and 2 per cent sales tax. With the drawback of 99 per cent allowed on the excise tax, the price per imperial gallon amounted to $2.99. The new ruling, however, compelling the hospitals to buy from the Liquor Control Board, fixes the rate per imperial gallon at $27.50, with a drawback of 99 per cent still available on the excise tax, a net price of $12.80 per gallon, or a difference of $9.81 per imperial gallon to be added to the hospitals' ever-increasing load.

The provincial government was approached by the British Columbia Hospitals' Association, asking for a repeal of this order, but were informed that there was nothing in the Act which would permit the hospitals to buy directly from the distilleries even though the hospitals had enjoyed such privilege for many years.

The matter is now being considered by a special committee of the Legislature and it is expected that an amendment will be made in the Act at the forthcoming session of the Legislature, which will permit the hospitals to buy ethyl alcohol direct from the distilleries.

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## Provincial Association Notes

### JUBILEE MEETING—ONTARIO MEDICAL ASSOCIATION

The Program Committee of the Ontario Medical Association, of which Dr. Geo. S. Young, of Toronto, is Chairman, has been meeting regularly since November 1, 1929, and has been successful in obtaining an unusual number of splendid speakers for the Jubilee Meeting, to be held in Toronto on May 27th, 28th, 29th and 30th, 1930.

The program will consist of general sessions held morning and afternoon during the days of the meeting. In addition to this, each of the five Sections will hold one sectional meeting. These sectional meetings are being arranged so that those particularly interested in any one section will not miss papers on the general session program which will be of special interest to them. In this way, it is hoped to increase the value of the meeting to the members.

Outstanding men from all the sister Provincial Medical Associations have been invited to take part in the program, as well as to represent their respective Associations. In this way we have been fortunate in obtaining notable men from other parts of the Dominion. Only a very few men from outside the Dominion have been invited to take part in our program, but, where exception has been made, those invited are men of outstanding reputation.

It is expected that a full program will be published in the next issue of the *Journal*.

In addition to the scientific program proper, arrangements are well under way to have displayed at the meeting a number of scientific exhibits of unusual interest. It is believed that these will add materially to the interest of the gathering.

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### THE ANNUAL MEETING OF THE SASKATCHEWAN MEDICAL ASSOCIATION

One hundred and fifty members attended the twenty-second annual meeting of the Saskatchewan Medical Association in Regina. Dr. F. H. Hurlburt, of North Battleford, in his address at the banquet, made a plea for the more adequate and systematic medical care of the poor; his ideas on this topic were progressive enough to be called radical by his more conservative listeners.

The technical addresses were all given by the visitors from the east. It was felt that if a speaker from Saskatchewan had been on the program the discussion following the papers would have been more frank. At the business meeting the training of medical students in eye refraction was discussed. A committee for the study of cancer was appointed, as follows: Dr. E. B. Alport, and Dr. C. M. Henry, Regina; Dr. R. H. MacDonald and Dr. E. E. Sheply, Saskatoon; and Dr. T. M. Leask, Moose Jaw.

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The following officers were appointed for next year: *Honorary President,* Dr. F. H. Hurlburt, North Battleford; *President,* Dr. W. A. Dakin, Regina; *First Vice-president,* Dr. R. A. McLurg, Wilkie; *Second Vice-president,* Dr. C. R. Totton, Assiniboia; *Secretary-Treasurer,* Dr. A. MacG. Young, Saskatoon; *Representative* to the Anti-Tuberculosis League, Dr. T. W. Walker, Saskatoon; *Representatives to the Council of the Canadian Medical Association,* Drs. W. A. Dakin, Regina; A. MacG. Young, Saskatoon; E. R. Myers, Saskatoon; L. A. C. Panton, North Battleford; H. H. Mitchell, Regina; J. H. Sharpe, Swift Current; S. M. Rose, Yorkton; J. F. Creighton, Estevan. *Editorial Board of the Journal,* Drs. Lillian A. Chase, Regina; Arthur Rose, Hafford; G. H. Lee, Shaunavon.

# University Notes

## McGill University

Important appointments and promotions were announced by the Board of Governors of McGill University at the final meeting of 1929. Among them are the following: Dr. B. Silverman, demonstrator in mental hygiene; Dr. B. F. MacNaughton, assistant demonstrator in oto-largyngology; Dr. H. M. Little, professor of obstetrics and gynæcology; Dr. J. R. Fraser, professor of obstetrics and gynæcology; J. W. Scott, assistant professor of bio-chemistry, replacing Dr. S. W. Bliss; C. F. H. Allen, assistant professor of chemistry, replacing Dr. G. S. Whitby; W. Barnes, lecturer in physics, replacing A. L. Patterson; Mrs. K. Pinhey, lecturer in zoology after an absence abroad for study; P. H. H. Gray, assistant professor of bacteriology at Macdonald College, replacing J. R. Sanborn.

The list of promotions is: Dr. E. M. Eberts, from associate to professor of surgery; Dr. D. L. Thompson, from lecturer to assistant professor of bio-chemistry; Dr. W. V. Cone, from lecturer to assistant professor of neurological surgery; John Beattie, from assistant to associate professor in the department of anatomy; J. S. Foster, from assistant to associate professor of physics; David Keys, from associate to professor of physics; W. H. Hatcher, from assistant to associate professor of chemistry.

It was decided that the financial campaign which was to have taken place next month would be left over for the time being.

## University of Manitoba

As was mentioned last month, the committee of the House appointed by Premier Bracken to report on the University site reported unanimously in favour of the Agricultural College site, and recommended that a building to cost one million dollars be erected thereon to provide for the needs of the senior classes in Arts and Science. For the time being the junior classes would be accommodated in buildings on the Broadway site. Much adverse criticism has been voiced in Winnipeg against the Agricultural College site, both on the grounds of distance from the city, and of the division of the University into junior and senior classes. Recently the Faculty of Arts and Science protested against this division. The report of the committee will, no doubt, be fully discussed at the next session of the Legislative Assembly in February.

## Bristol University

On December 13th the Right Hon. Winston Churchill, P.C., C.H. was installed as Chancellor of the University of Bristol, in succession to the late Lord Haldane. The ceremony took place in the Great Hall, and it is interesting to record that Mr. Churchill wore the black and gold robes which had been used by his father, Lord Randolph Churchill when Chancellor of Manchester University. The Right Hon. Henry Hobhouse, the senior Pro-Chancellor, welcomed the Chancellor on behalf of the University and installed him, presenting him with a key of the University Seal and a copy of the University Charter. The Vice-Chancellor presented Mr. Churchill with a patent of the degree of Doctor of Laws, after which the new Chancellor proceeded to confer the honorary degree of Doctor of Laws upon Miss Margaret Bondfield (Minister of Labour), Mr. Philip Snowden (Chancellor of the Exchequer), Admiral Sir Roger Keyes, Mr. Walter Runciman, M.P., and Dr. Thomas Sibly

(Vice-Chancellor of Reading University), and the honorary degree of Doctor of Letters was conferred upon Mr. Walter de la Mare and Dr. Vaughan Williams.

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Dr. R. J. Brocklehurst has been appointed to the chair of physiology in the University as from August 1st of this year.

A medical graduate of Oxford, where he took a first-class in the honours schools, Dr. Brocklehurst worked as assistant in physiology, first part-time, then whole-time, at St. Bartholomew's Medical College from 1925 to 1926. He was then awarded a Radcliffe Travelling Fellowship, with which he went to America and Germany. In August, 1928, he returned to take up the post of senior lecturer in physiology at University College.

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### University of Aberdeen

The Regius Chair of Medicine, which is now vacant and which is the oldest foundation for the teaching of medicine in Great Britain, has been a part-time one at £850 a year. Henceforth it is to have a salary of £1,200 attached to it, in view of the professor being expected to devote more of his time than hitherto to teaching and research, while additional assistance and facilities for research are to be provided. The holder of the Chair is an Honorary Physician to the Royal Infirmary of Aberdeen, with charge of beds. The appointment to the Chair is made by the Crown on the recommendation of the Secretary of State for Scotland.

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## Topics of Current Interest

### The Relation of Physiology to Clinical Medicine

Physiology is the keystone in the arch of medical and surgical knowledge. On its security depends the security of the superstructure of medicine as a science. Physiology is primarily a study of life. Human physiology is therefore a study of human life. Physiology must be studied on living organisms, or on living parts of the organism. A knowledge of the subject is based on experiments that can be performed on man or on animals showing functions resembling those of man. The human animal should be used so far as possible in the training of medical students. Probably in no other science does the student encounter as many theories as are found in physiology. These theories represents gaps in our knowledge which must be filled in by patient research. It is therefore highly important that every physiologist must be an investigator. Physiology cannot be properly taught as a series of essentially unconnected facts. Co-ordination and co-operation are major principles in the proper functioning of any organism, just as they are in any complicated and smoothly working machine. If one is to gain a thorough understanding of the organisms or the machine one must thoroughly understand the interrelations of all its parts. It may be a mistake to permit students to purchase a textbook. A teacher with a broad and thorough knowledge of the subject might be able to give a clearer picture and bring about a better co-ordination of the subject. The teaching of physiology should not be limited to the brief course given in the first or second year. Throughout his medical course, the medical student should be made conscious of the fact that he is constantly dealing with physiological principles. It should be the duty of every clinical teacher to impress on his students the need of daily application of their knowledge of physiology to their clinical problems. When this is done, clinical medicine will become more definitely the sciences of medicine. There is too much of a tendency on the part of the teachers of laboratory sciences to hold themselves apart from clinical medicine. The teachers in the first two years should be on the staff of the teaching hospital and should take an active part in the staff meetings and in consultations in the hospital. The laboratory man should not be considered a mere technician. Every teaching hospital should furnish facilities for clinical research, preferably in close co-operation with the laboratory departments. The clinician should be encouraged to devote a larger portion of his investigation to the living organism rather than merely to satisfying his curiosity in the autopsy room. A more careful study and application of physiology would illuminate many of the dark corners of clinical medicine. The progress of physiology goes hand in hand with the development of clinical medicine and there is a mutual interdependence. The experimental method is used jointly by the modern physiologist and the modern clinician, and in the use of this method the clinician becomes a physiologist. Physiology is not a stepping stone to clinical medicine. It is clinical medicine.—Maurice H. Rees, abstract from the *J. Am. M. Ass.*, **93**: 739, September 7th, 1929.

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### The Critical Condition of the Medical Profession

Prof. Schlossmann, of Düsseldorf, lately read a paper before the German Society for Social Hygiene on the crisis in our profession. The liberty of the medical man, he said, is a dream of days gone by and the profession cannot longer resist a progressive nationalization. Apart from some specialists with a large income the majority of doctors earn their livelihood from the fees paid them from institutions under the State Insurance Act. This Act provides them with 250,000,000 marks every year. Moreover, the individual practitioner has to observe so many rules and regulations issued by the government and by insurance authorities that he cannot be described as a free worker. Prof. Schlossmann does not at all agree with the leaders of the profession in their fight against sick clubs and other institutions of State insurance, for he holds that it only embitters their mutual relations. It would be better, he thinks, to co-operate with them so as to get over certain abuses.

According to Prof. Schlossman, the profession is suffering from an economic crisis, an ethical crisis, and a crisis of confidence. The position of the younger generation who have to wait several years before admission to club practice is desperate financially, but still worse is the fact that they are obliged to be without work at a time when it is most desirable that they should be gaining experience and consolidating what they have learnt. The present method of study does not create medical practioners; two years are spent in learning chemistry, physics, botany, zoology, physiology, and anatomy, and during this time the medical student does not see a single patient. Furthermore, clinical teaching is much too theoretical. What is worst of all is the public lack of confidence in doctors. The Insurance Act leads the patient to look upon the practitioner as more of a sick club officer than a medical adviser. Medicine has changed from an empirical to a technical science. The individual practitioner is not in a position to know all the technical methods of treatment and still less to provide for himself all the technical apparatus; this is the reason why patients are often sent to dispensaries, hospitals, and clinics, which have modern equipment. The increasing number of unqualified persons and the afflux of patients towards them bear further witness to the critical state of the profession.

Prof. Schlossmann suggests not that social insurance should be limited but rather that it should be extended. The object of sick clubs should be not only to cure their members but also to keep them in good health. If this were done, and if those classes of the population who are still outside national insurance were admitted to its benefits, a great number of the profession would find employment. His address has created a sensation, for he is a man who is well known in his specialty and also as president of the successful exhibition of hygiene held in Düsseldorf in 1926. The *Arztliche Vereinsblatt*, the official organ of the Vereinsbund, says that his opinion that the representatives of the profession are hostile to State insurance is absolutely erroneous. But the medical profession, it continues, wishes to remain a free profession whose rights and duties as to insurance practice are limited by free agreement, and it is not inclined to become a mere collection of insurance employees. — Berlin Letter, *The Lancet* **5544**: 1165, Nov. 30, 1929.

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### Another Experiment in Middle Class Medical Care

In February, 1930, the trustees of the Massachusetts General Hospital will open a new unit called the Baker Memorial. The Rosenwald Fund Committee has agreed to underwrite one-half of the deficit in operation of this hospital during its first three years up to a maximum of $150,000, with the understanding that the deficit will not exceed $75,000 in any one year. The Baker Memorial has been designed for the care of sick people of moderate means. It is pointed out in the *Massachusetts General Hospital News* that the care of the sick in this unit will include voluntary curtailment of physicians' fees so that those entering the institution will pay a maximum fee of $150 for any illness or operative care and that the maximum fee for uncomplicated obstetric service and hospital care will be $100. Only members of the staff of the Massachusetts General Hospital and of the Massachusetts Charitable Eye and Ear Infirmary and the obstetric staff will be permitted to practice in this institution. This hospital has been definitely planned and constructed, and is to be quite definitely operated, as a middle class institution. The employment of special nurses will be discouraged. Ward maids, nurses' helpers and floor clerks will be utilized so that nurses will devote all their time to actual bedside nursing. A special social service department will control the class of patients to be admitted. The institution will have 333 beds, part of which will be used at first for the internes and the nurses, since special buildings for this purpose have not yet been provided. There are to be eighty-eight beds in single rooms, twenty-four beds in two-bed wards, twenty-eight beds in four-bed wards, and eighteen beds in cubicles. For obstetric patients there will be twelve beds in single rooms, six beds in two-bed wards, and eight beds

in four-bed wards. Private rooms will cost $6 a day, cubicle beds $4 a day, and the two-bed and four-bed wards will vary between these figures. Nursing, food and ordinary drugs are included in this price. Special fees will be charged for laboratory work and for roentgen-ray work. It will be interesting to see whether this experiment can operate successfully and pay its own way. It will also be interesting to see whether there s any considerable percentage of the middle class who can save enough money to take care of themselves under these conditions. The fees are not apparently much greater or much less than those charged to-day in most of the hospitals in the United States.—*J. Am. M. Ass.* 93: 1891, Dec. 14, 1929.

## The Etiology of Influenza

The *Journal of the American Medical Association* publishes (page 2030) a preliminary report of the work by I. S. Falk, Ph.D., and his colleagues on the etiology of influenza. The University of Chicago investigators do not seem to have gone far beyond previous research on influenza, as was pointed out in our current comment last week. The difficulty in interpreting the results is largely due to the fact that it is difficult to distinguish clinical epidemic influenza from acute respiratory infections in monkeys and, indeed, in man. In 1892 Pfeiffer described an organism as the causative organism of this disease. Since that time other allegedly causative organisms have been described. In a review of the history of the bacteriology of influenza by Prof. E. O. Jordan,* it is revealed that every decade since 1900 has yielded its quota of influenza germs. The earliest definite report of successful human inoculation with pure culture of the Pfeiffer organism was recorded by Dr. D. J. Davis in Chicago in 1906. Davis, however, emphasized that the symptoms following inoculation in human beings were not those of true influenza. During the 1918 epidemic, volnnteers were inoculated with thirteen different strains of bacteria isolated from cases of influenza. All developed symptoms, but again it was believed that these symptoms were not the typical symptoms of epidemic influenza. The green producing streptococcus isolated by Mathers and Tunnicliff in 1918, the one isolated by Rosenow of the Mayo Clinic in 1919, the filter passing organism described by Meyer in 1919, and the organism discovered by Olitzky and Gates of the Rockefeller Institute and called by them *Bacterium pneumosintes*, would seem to deserve as much consideration as should be given, at least on the basis of the available evidence, to the germ recently announced by Falk as the specific cause of this disease. Jordan wisely emphasizes, after a consideration of all the available facts, that it cannot be definitely asserted that negative inoculation experiments are sufficient to rule out Pfeiffer's organism, since it is quite possible that there are some unknown factors which influence the likelihood of a person to become infected with influenza. The work of Falk and his colleagues is of great interest and should, no doubt, be given serious consideration in any survey of the bacteriology of influenza. To intimate, as was done in numerous interviews, editorials and other publicity relative to this discovery, that the way is now clear for a vaccine or antitoxin or any other specific method of treating influenza is to go far beyond the actual evidence provided by this bacteriological research.—*J. Am. M. Ass.* 93: 2034, Dec. 28, 1929.

* Jordan, E. O., Epidemic Influenza, Chicago, American Medical Association Press, 1927.

## Clean Air

The National Smoke Abatement Society has produced a new journal called *Clean Air*. The first issue, dated Autumn, 1929, is sent forth with good wishes from many eminent people, and contains a number of articles on the purification of the atmosphere in our cities. Smoke was long regarded as the inevitable accompaniment of industry, and the possibility of freeing the air from it was at first the fad of a few. The idea has, however, taken firm hold and may very soon become the normal expectation of us all. It has been demonstrated over and over again in industry that the most hygienic method is the most economical, and cleansing of the atmosphere obeys this law, for smoke is simply wasted fuel. There are three principal lines along which to proceed with smoke prevention: gas, electricity, and smokeless fuels like anthracite. *Clean Air* contains an article on the use and development of gas in industry, giving examples of the innumerable directions in which gas can be economically used in various trades. The director of a research institute in America has estimated that the potential market for industrial gas is at present only 2 per cent saturated. Another article deals with the uses and development of electricity in industry and stresses its very wide range of application, its precise and positive control, the exceptional uniformity of temperature which it yields, and the reduction to a minimum of labour requirements. It must be admitted, however, that the private consumer is the chief offender against the purity of the atmosphere; regulations have already gone far towards abolishing the cloud of smoke that used to belch forth from factory chimneys, but every small house contributes its little wisp

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to the fog that lies over London. The annual review of domestic heating given in the new journal suggests that those who long for the comfortable sight of an open fire burning in the grate should have their wish—more or less—by burning either anthracite or high quality gas coke in their grates. The low-temperature carbonisation fuels have saved the open grate from the condemnation with which it was threatened by the reformer, and though it must be admitted that such fuel still remains rather more expensive than coal, it reduces dirt and labour in the house as well as smoke outside it. Much experimental work requires to be done on these combustibles, and there is also scope for improving the general temperature of British houses by central heating or by insulation, so that the amount of fuel burned in the open grate is reduced. There is a very great deal to be said for the abolition of smoke, and practically nothing except prejudice or sentiment (and the price of smokeless fuels for those who want the open grate) to be said against it. We hope that the new journal will receive the support for which it asks and will be able to carry the campaign for clean air into the homes and factories of the whole country.—*The Lancet* **2**: 1271, Dec. 14, 1929.

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### Disease Germs in the Upper Air

Remarkable experiments proving that disease germs are carried and epidemics spread by the thin air currents of the upper atmosphere have just been completed at Cambridge. The work has been directed by Mr. W. A. R. Dillon Weston, M.A., of the University School of Agriculture. In association with Mr. Everett, of the Hampshire Light Aero Club, and Flight Lieutenant Goddard of the Cambridge University Air Squadron, he has been chasing bacteria by airplane and catching them by the million in traps. Three kinds of germ traps were used—glass slides smeared with petrolatum, test tubes containing culture mediums, and glass dishes also filled with a culture medium. They were taken up sealed in the airplane, unsealed and exposed when the desired height was reached, and then sealed again. The principal object is to trace how diseases of plants and crops can be spread through the upper atmosphere. Dr. Dillon Weston was not concerned with animal and human diseases. It was proved that spores and bacteria may be found at great heights and yet retain their vitality. With test tubes containing a culture medium, 40 per cent of the exposures were positive. The highest altitude at which the traps were exposed was 13,000 feet.

A particularly interesting flight was made from Duxford to Cambridge in May, at an altitude of 2,000 feet. Three plates were exposed for a period of one minute. On arrival at Cambridge the machine was put up to 4,000 feet, and three exposures were taken on the return journey. It was impossible to count the contaminations of those exposed on the outward journey. Many hundreds of spores and bacteria must have alighted on the culture medium. The plates exposed at 4,000 feet were much less heavily contaminated. A comparison with flights in the winter months shows that in summer the air is much more heavily charged with bacteria. The results obtained show how local epidemics of plant and animal diseases may be brought about and the ubiquitous nature of bacteria and of fungus spores in the upper air. Large numbers of these bacteria are active even at a height of two miles above the earth. The clouds were more heavily charged with spores and bacteria than the air a little below them. The work suggests that the air is the ideal medium for the transportation of disease organisms.—London Letter, *J. Am. M. Ass.* **93**: Sept. 7, 1929.

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### The Press*

The press and the medical profession in some respects are opposed to each other, for the former lives and has its being by purveying publicity, while the latter must by the nature of the functions it performs be restrained and discreet. A common ground of agreement between these opposite aims is somewhat difficult to discover, but I am inclined to think that health propaganda is perhaps the one subject in which the two can co-operate wholeheartedly. We both ardently desire to improve the health of the nation, and we must frankly admit that neither of us can do much in this direction without the help of the other.

I hope this conference will pardon a personal reminiscence, but I relate it only in order to put myself on good terms at the outset with my audience. I am, in a way, a pioneer, for in the year 1913 I published a letter courageously signed by some of the greatest men of your profession, drawing attention to the grave consequences of the ignorance of the public on the subject of venereal diseases, especially syphilis. It was urged upon me by many eminent doctors and surgeons that such an indictment of our apathy and indifference was necessary in the interests of the nation. I took what little courage was left me by my friends in both hands, published the letter, and supported it warmly with a leading article. The result was that in a short time a matter of great and even vital

* Read in a discussion in the Section of Medical Sociology at the Annual Meeting of the British Medical Association, Manchester, 1929.

importance to health was openly discussed and is now no longer confined to the technical columns of the medical press.

It may therefore be taken for granted that the press is only too anxious to march side by side with medicine in the fight for public health. Yet, in spite of this, there are some obstacles to be overcome before we can act together with complete understanding. The press will help in the good work, but it will always want to do so in its own way. The medical profession, bound and tied by strict rules and regulations, would like it done in its way, and there comes the first difficulty. Every newspaper seeks to have an individuality of its own and to carry this individuality right through its pages. For this reason, the concentrated wisdom of all the doctors, if it be distributed to the press generally, will be set aside in favour of the contribution of a lowly general practitioner with a lively pen. Let not this be counted against my profession. I have known of cases where a good-looking doctor with tenuous qualifications has snatched away the women's portion of the practice of his colleagues in a few months.

Health is a matter of intense interest to everybody, and journalists, having quickly grasped the fact, are naturally eager to provide their readers with the best information they can. In the search for this they often find themselves face to face with the strict rules and regulations of the medical profession. Like many other institutions, such as the Law Society and the Stock Exchange, members are forbidden to advertise, and it has, I believe, been laid down that a signed article in a lay paper is an infraction of this rule. We are thus brought to an impasse. Newspapers require articles at odd times and on odd subjects. They search out the best specialist on the particular subject required, and in nine cases out of ten meet with a ready, not to say eager, response. Then comes the difficulty. It must not be signed by the author—that would bring the wrath of the gods on his head. The article is therefore published as from "a distinguished Harley Street specialist," and all we get for our pains is a series of letters from our readers accusing us of inventing the specialist and writing the article in the office.

Any fair-minded journalist will readily grant that it would not be in the interest of medicine generally that doctors should advertise. It certainly would add to the attraction and revenue of a journal that Dr. X. should use the advertising columns to announce that he would "undertake to make the most melancholy sing in his bath," or that Dr. Y. should say to the world "Don't let them cut you up; let Nature and Dr. Y. put you right without an operation." One's imagination soars at the thought, and, like Clive, we are amazed at our moderation in not starting a press campaign in favour of the abolition of this rule.

Still, there is the problem. We journalists want authoritative information in a hurry, with a name at the top of it, and you of the medical profession would rightly see in that a dangerous innovation which might do infinite harm. It is to be remembered, however, that several eminent doctors do contribute to the press under their own names and no protest appears to have been made by the General Medical Council. Doubtless you might argue that this small band of privileged writers should suffice for the needs of newspapers; but in point of fact they are not numerous enough to fulfill the requirements of the newspaper press to-day. It seems to me that the British Medical Association might well examine this matter and see whether it cannot evolve a solution of the difficulty. As things are at present I am convinced that medicine is losing many great opportunities of teaching the people the great lessons of health, so essential for the well-being of the country.

A cynic once remarked that one of the reasons why a doctor is called in is because the patient has the rare and refreshing opportunity of talking about himself and being heard with attention. Whether that is true or not the fact remains that there is nothing quite so interesting to newspaper readers as discussions on health. Rarely a day passes without a letter being received from a reader asking how best he or she can get fatter or thinner; acquire an appetite or lose some of the craving for food, where to find the best brand of vitamins; whether a whisky-and-soda at bedtime is good for insomnia; or which is the best doctor to consult for persistent halitosis. To our credit be it said that our invariable answer is "Consult a doctor," and in the last case the reply was "Consult any doctor." Such daily experiences are conclusive proofs of the fact that medical matters are, in the language of our craft, "good copy," and therefore it needs no stimulus from outside to quicken our interest in them. However pontifically we may speak to the public on a great variety of subjects, we are quick to realize that it is highly dangerous to pronounce opinions on matters that concern the physical health of our readers. To help us we must turn to your profession, and often in vain.

It might well be suggested that, if there exist such an interest in medical matters among the newspaper reading public, it would be to the advantage of journalism to have a doctor on the permanent staff as general adviser and writer on all that concerns medicine. This suggestion may have been put into practice, though personally I cannot recall any instance of its adoption. There are objections to it which are

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fairly obvious. In the first place it is possible that a qualified doctor who accepted such a position on the staff of a newspaper might be running foul of some of the conventions of the General Medical Council. Even if it was otherwise, I am somewhat doubtful whether such an experiment would succeed. One of two things would happen: either the medical correspondent would absorb the spirit of his environment and become more of a journalist than a sober *terre-à-terre* doctor, or he would retain the restraint, reticence, and admirable dignity of his profession and be useless as a member of the staff of a newspaper. Besides all this, I doubt very much, except in cases of young doctors still in search of a practice, whether the career of journalism would be tempting enough for a man who has spent four to six years to qualify. It would be a bad thing for both medicine and journalism if incompetent men were engaged.

Owing to the restrictions to which I have referred we journalists are limited in our endeavours to act as interpreters for your profession to the people. We are driven, therefore, to the published words of eminent physicians or surgeons over whom the General Medical Council does not seem to exercise control. Here we are met with the difficulties of such a divergence of opinion as to render our efforts nugatory. Take diet for example, Sir A.B., a physician with a most distinguished record, says alcohol is poison. Sir B. C. makes a speech and pronounces it to be a most excellent and salutary stimulant when taken in moderation, and confesses that he himself always takes a nightcap. "Beer," says Sir D.E., "is both drink and food. Taken in moderation it is an excellent digestive, a magnificent and safe pick-me-up, and should be on every table in the land." Whereupon Sir F.G. declares that if a man has any sort of regard for his liver, he should not even smell an empty beer-pot, much less drink the vile stuff. If people will drink, let them drink light wines, whisky, or egg-flip. Who shall decide when doctors disagree?

So far, I am afraid that you will think that I have been a little lukewarm in my advocacy of joint action between the doctors and journalists. This, however, is not the case. If I have mentioned particular circumstances under which co-operation between the two has been somewhat difficult, I have no hesitation whatever in declaring that on the broad question of the presentation of the plain facts of health there can be, and there should be, the most hearty and constant collaboration of the two professions.

There will be moments in our national life when disaster can only be averted by the combination of medicine and journalism. Epidemics may rage again, and the people will require daily warnings and advice. When this happens I feel sure that the doctors can call on the press to help, and that call will receive an immediate and enthusiastic response. The seasonal ills of spring, summer, autumn, and winter are topics of interest to the press, and we gladly receive and print the advice so generously placed at our disposal by your great profession. Every day there is made some advance in the great science of medicine, and if, as is right and proper, you are reluctant to raise hopes too soon, or to divulge a secret until it has been thoroughly tried out, we too, are willing to keep silent until the right time for discovery has come. To enforce the simple rules of health which are approved by your profession, to save the people from expensive and dangerous quacks, to do all that is in our power to make of our people the healthiest, as they are the sanest, in the world—these are noble aims worthy of the great professions to which you and I belong.—H. A. Gynne, President of the Institute of Journalists in *Brit. M. J.* **2**: 244, Aug. 10, 1929.

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Professor Hill, of the Department of Applied Physiology, National Research Council, London, points out that the wide-spread explanation in the past as regards discomfort and impaired health from crowded and ill-ventilated rooms and apartments is erroneous. It is not an excess of carbonic acid gas or lack of oxygen, or the presence of organic impurities in expired air; the real cause is not chemical but physical. The great value of open-air treatment is the result of the heat produced by the sun, plus the cooling and evaporating influence of the outdoor air in motion. Hence this efficient regulation of the body heat by the evaporation process and the current of air experienced outdoors, rapidly changing the volume of air surrounding the individual, increases absorption and elimination and also stimulates digestion. Professor Hill goes on to say that the open-air treatment of tuberculosis upon which so much stress has been placed, should be based on physiological principles and not on a blind belief in the virtues of fresh air alone, and in conclusion he says, "The old carbonic acid gas idea as a gauge of atmospheric purity is a thing of the past and, together with the organic impurities so frequently referred to, may be placed in the museum of archaic ideas."

# Special Correspondence

## *The London Letter*

*(From our own correspondent)*

Amidst a succession of sensational failures on the stock exchange many a prosperous practitioner is hesitating as to the best means of investing his money. If the latest fashion in medicine is at all a trustworthy guide he would be well advised to buy shares in a glucose factory or invest in a reputable barley sugar firm. Dr. H. C. Cameron is probably to a great extent responsible for the beginning of the modern craze for glucose, for in his admirable descriptions of the nervous child he has on more than one occasion pointed out how recurrent attacks of acidosis are intimately related on the one hand with the child's nervous system and on the other with a shortage of available glucose in the child's blood. The type of nervous child which Dr. Cameron describes is certainly on the increase since the war, often labelled by the older generation of children's physicians as "T.M.", or "typically modern", and certainly such children benefit from a diet containing less fat and more sugar. The glucose craze has, however, been pushed to an absurd degree in some quarters. Because certain cases of asthma in children occur in the same nervous type of child and therefore benefit from the administration of glucose, the absurd statement finds its way into the press that all asthma can be cured by glucose and "a clever young chemist, etc.," . . ."the most important medical discovery of the century." Dr. Cameron has performed a valuable service in pointing out the metabolic side of the child's mind, so to speak, but this view can be pushed to an extreme as was illustrated in an important recent discussion on "The Difficult Child" at the Royal Society of Medicine. The work of the child guidance clinics was fully discussed and while the general state of the child's physical well-being and metabolism is recognized as important, it is by no means the whole story. One psychiatrist quoted the example of the child who is an "angel in the home" and "a perfect devil at school" and he found this difficult to explain "as a vagary of a carbohydrate molecule". Glucose is being shovelled into many children nowadays in a wholly indiscriminate fashion and even adults have not escaped the craze.

Last year saw a renewed interest in the diseases due to the inhalation of dust and especially the comparatively new disorder of pulmonary asbestosis attracted attention. For the ordinary individual these pulmonary disorders have little importance, but he is concerned with the possibility of disease from the atmosphere he breathes. The increase of cancer of the lung has been ascribed by some authorities to the widespread use of tar on all the modern roads, and in a recent article two doctors have called attention to the prevalence of arteriosclerosis among coal-miners, due they think, to the high tension of carbon dioxide in the air of mines. Twenty years ago, Drs. D. E. and W. A. Dickson, working in Fife, noted that arterial thickening was especially common among coal-miners even in quite young men. They have since investigated five hundred cases and in certain fatal accidents have been able to establish the existence of a marked degree of thickening of the inner coat of the arteries. Such thickening is not associated with any rise in blood pressure, but may have something to do with the way in which miners die off somewhat rapidly after the age of 55, as compared with other workers. The various possible factors thought to account for this arteriosclerosis have been investigated and the atmospheric conditions under which the miners work seem to have been definitely incriminated. This has a bearing on our general mode of living, for, as was pointed out in a recent protest to *The Times*, we are becoming careless about ventilation, and the atmosphere of many a modern flat, to say nothing of the cinema, contains too much carbon dioxide to be considered comfortable for health. Possibly it is in this that the explanation lies for the increase of arteriosclerosis among the whole population.

The mother hospital of the British Empire, founded more than eight hundred years ago, has come to the public for help and the Prince of Wales recently inaugurated an appeal by St. Bartholomew's Hospital for a million pounds. This sounds a very large sum, but "Bart's" is near enough to the heart of the City of London in more ways than one, and there is every hope that the appeal will be successful. Bart's has already erected a big new surgical block and the nurses' home is being enlarged. A great new out-patients' department has already been built and much more remains to be done. Children are at last to be looked after in a separate department, and various other special departments will receive attention, while the medical school is to be brought up to date. Bart's has a world-wide fame and its new buildings will enhance its justly won reputation.

ALAN MONCRIEFF

London, January, 1930.

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## *The Edinburgh Letter*

*(From our own correspondent)*

The bicentenary of the Edinburgh Royal Infirmary was marked by a commemorative service in the Cathedral of St. Giles on November 27th. Two hundred years ago this hospital was founded. The first building was a small house in Robertson's Close, on the southern slope of the valley of the Cowgate. Until the opening of this—the Old Infirmary—no other establishment in Edinburgh had been devoted to the purpose of caring for the sick poor. During times of strife and turmoil buildings had been commandeered and utilized as military hospitals, as when Cromwell quartered his sick and wounded soldiers in George Heriot's School. In those days the poor received scant attention when they were sick. The hospital in Robertson's Close was the result of an appeal by the College of Physicians—an attempt to relieve the existing conditions under which 40,000 inhabitants lived huddled together in narrow wynds and noisesome closes clustering round the Royal Mile, in houses entirely devoid of the crudest elements of sanitation. Two thousand pounds were raised for this first venture. So successful was the scheme that in 1738 the foundation stone of a new institution was laid in Infirmary Street. This new hospital was completed and opened in 1748. Here it was that Professor John Rutherford and his colleagues introduced the method of bedside teaching, modelled upon the practice that had pertained at Leyden for a century before. A hundred years ago, in 1829, the institution was greatly extended when the High School was moved to its present site on Calton Hill. The school buildings were adapted and furnished as the "Surgery Hospital", later to become so intimately associated with the surgical work of James Syme and Joseph Lister. As the fame of the hospital spread abroad, the demand for beds increased steadily. Patients came from all over Scotland and much of the north of England. As far back as 1853, the number of patients accommodated in the wards was 4,600 for the year. In 1879 the present hospital in Lauriston Place was opened at a cost of more than £350,000. This year, 1929, is therefore not only the bicentenary year of the original hospital, it is also the Jubilee year of the New Royal Infirmary. At present the hospital has more than 1,000 beds. During last year 19,680 patients were treated in the wards, while 62,085 out-patients received medical and surgical aid. Recent additions to the institution include the new Radiological Department, costing £50,000, opened by the Duke of York in 1926, and a clinical research laboratory, gifted by the Rockefeller Trust at a cost of £35,000. The Infirmary cannot afford to stand still. Further developments are foreshadowed. Just as one hundred years ago, the Royal High School, by moving out, made room for the former "Surgery Hospital", so to-day, a large extension is to be built on ground shortly to be vacated by George Watson's Boys' College. This scheme is to provide a maternity and gynæcological hospital for the accommodation of 240 patients. It is estimated that this new department will cost £300,000. The Edinburgh Royal Infirmary is the largest voluntary institution of its kind in the British Isles. It was founded for the purpose of "The saving and restoring to health of members of society", and the education of the future medical practitioner. These two functions it has honourably and faithfully performed. "Patet omnibus" has been and is its motto, and to its ever open doors have flocked an always increasing crowd of sufferers. It has been the centre and stimulus of the Edinburgh Medical School. Since 1748 clinical teaching has been conducted in its wards. Here have lectured those famous physicians and surgeons, whose reputations as teachers, workers, and discoverers have attracted, and still attract, students from all over the world. It is not only the inspiration of Medical Edinburgh, it is the soul of a much wider community. Its aspirations and ideals rouse such a sympathetic appeal that one of its proudest claims to fame is that there are more than 120,000 persons subscribing regularly and systematically to its funds. Many of these are the fishermen of the Forth, the miners of Fife, and the farm labourers of the Lothians, who are anxious to show their appreciation of this great and voluntary undertaking. The service in St. Giles Cathedral was conducted by the Dean of the Thistle and Chapel Royal. It was attended by the Lord Provost and Town Council of the city, Senators of the College of Justice, the Senatus of the University, the Councils of the Colleges of Physicians and Surgeons, and representatives of many other public bodies.

A valuable history of the Royal Infirmary with its two hundred years of development and progress has been written by A. Logan Turner, LL.D. Those who are familiar with "Joseph, Baron Lister," by the same author, will realize that the Infirmary is fortunate in its historian. This interesting record deals with the Foundation of the School of Medicine, the Early Hospital, Clinical Teaching, and the Rise of the Medical School. It is concise and clear, written in Dr. Turner's best style and with the painstaking regard to historical accuracy that characterizes all his work. This worthy addition to the library of books dealing with medical history in Edinburgh is well illustrated with nine pictures and two plans. The proceeds from the sale of this remarkable narrative of achievement are going to the Infirmary funds. This handsome

volume is published by Oliver and Boyd, Tweeddale Court, Edinburgh.

The 16th-5th Lancers have recently arrived in Edinburgh from Salisbury Plain and are stationed at Redford Barracks. They are commanded by Lt.-Col. Joseph Lister Watson Cheyne, the elder son of Sir William Watson Cheyne, Lord Lister's old assistant. Sir William, who is Lord Lieutenant of the County of Orkney and Shetland, lives on the Island of Fetlar in the Shetlands.

On December 14th, a Memorial to the late Dr. John Thomson was unveiled at the Royal Hospital for Sick Children. The ceremony was performed by Sir Thomas Barlow, Bart., K.C.V.O. The Memorial is in the form of a marble panel, with an inscription and a bronze portrait medallion, the work of Mr. C. O'D. Pilkington Jackson, sculptor. At the same time a medal has been presented to the university for a thesis or original investigation of special merit dealing with children.

On Sunday December 8th, a Memorial to the late Major-Gen. Sir William Grant Macpherson, K.C.M.G., R.A.M.C., was unveiled by Gen. Sir William Peyton, K.C.B., commanding the troops in Scotland, Lt.-Gen. Faweus, C.B., the new Director-General, Army Medical Services, and Major-Gen. Barrow, C.B., Director of Hygiene at the War Office, travelled up from London to attend the ceremony. The R.A.M.C., regular and territorial units, paraded at St. Giles' Cathedral for the service, together with representatives of the Fettes College Cadet Corps—General Macpherson's old school. Canadians will remember "Tiger" Macpherson as D.M.S. to the First Army in France, and as D.M.S. to the Army at Salonika. He was later Deputy D.G.M.S. to the British Army in France. After his retirement he edited the official medical history of the War. On the Saturday night preceding the unveiling, General Peyton and Lieut.-General Faweus were entertained to dinner by the officers of the Territorial R.A.M.C., Edinburgh District.

GEORGE GIBSON

23 Cluny Terrace, Edinburgh.

# Letters to the Editor

## Carbohydrate Metabolism

*To the Editor:*

I have read with much interest your article on the Recent Studies in Carbohydrate Metabolism based upon Macleod's London lectures printed in the *Lancet*. It may interest you, in this connection, to look over the new theory of a cellular as well as a pancreatic insulin which I have proposed recently. This helps to explain much of the riddle of carbohydrate metabolism. If there is a further supply of insulin in the body which we have been taking no account of, then all of the results so far obtained from depancreatized dogs, such as the D:N ratio; and all facts concerning the utilization of glucose obtained from protein, and the formation of glycogen from this glucose after removal of the pancreas, must be reconsidered in the light of this new insulin, which makes unnecessary the purely speculative theory of gluconeogenesis which is advanced to make possible the further theory that the extra sugar, exceeding the amount possible from protein, must come from fat.

The theory of gluconeogenesis is in violation of one of the best established laws of carbohydrate metabolism, which is that glycogen can only be formed by the action of insulin on glucose. My new theory claims that there is a quantity of cellular insulin always present in the animal after removal of the pancreas and this makes possible the formation of muscle glycogen from the blood sugar. Furthermore it obviates the necessity of supposing that sugar must be obtained from fat as Macleod claims. He attempts to prove his contention by the frequent injection of epinephrine, thus producing more sugar than can be accounted for by protein, and hence supposing, although this is only speculation, that the extra amount must come from fat. But here again something has been overlooked. If, in the tissue cells which form the great vacuum for sugar, there is insulin as well as glucose, then it follows inevitably that glycogen is there in quantity. Now the general action of epinephrine is to cause glycogen to be re-converted into glucose—everywhere. It first releases it in the liver which supplies it to the blood current, and then if more is called for the glycogen stores of the tissue cells are called forth, and it is from this source, after the liver has been cleared of glycogen, that the large amount of sugar comes which appears after frequent injections of epinephrine, although Macleod claims this must come from fat. If these injections were continued long enough, even muscle glycogen might be released, but in that event of course the heart and respiratory muscles must stop work.

The relationship of glucose to insulin and epinephrine in carbohydrate metabolism may be expressed by the following rule:

Insulin forms glycogen from glucose, while

epinephrine causes the formation of glucose from glycogen.

Thus the machine may go forwards or backwards. And it may be said that insulin produces its results through enzyme or hormone action, while epinephrine is controlled by nerve influence through the splanchnic nerve and the medulla of the suprarenals.

Conclusion. There is no evidence that glucose is derived from fat. The theory of gluconeogenesis is contrary to established principles.

Sincerely yours,

South Acton, Mass., Oct. 12, 1929.

GEO. H. TUTTLE

# Abstracts from Current Literature

## MEDICINE

**Observations on the Etiologic Relationship of achylia gastrica to Pernicious Anæmia.** Castle, W. B., *Am. J. Med. Sci.* **178**: 748, Dec. 1929; and Castle, W. B., and Townsend, W. C., *ibid.*, 764.

The authors have investigated the relationship of achylia gastrica to pernicious anæmia by an ingenious and entirely novel method. They began by testing the effect on pernicious anæmia patients during a state of severe anæmia of beef muscle which had been predigested in a normal human stomach . The technique was as follows. Normal individuals, mostly students and physicians, were given a meal of 300 grams of nearly raw Hamburg steak. After an hour, vomiting was induced by pharyngeal stimulation. The vomitus was incubated for some time at body temperature and the acidity maintained constant by adding concentrated HCl. This material was given daily to the patients with a severe anæmia, by means of a Rehfuss tube. The diet during this time excluded liver, kidney, and meat. The effect was in all respects comparable to that observed when liver is given, namely a sharp rise in the reticulocytes about the tenth day, followed by a rise in the erythrocyte count. During control periods when the steak was given without predigestion no such effect was noted.

The next step in the investigation was to obtain normal fasting gastric juice by histamine injection and to incubate this *in vitro* with Hamburg steak. After incubation this mixture was inserted into the stomachs of patients under conditions similar to those in the first experiments. Again the patients showed a favourable response. Normal gastric juice after incubation alone failed to produce this effect.

In the final series of experiments, the Hamburg steak and the normal gastric juice were incubated separately, and were given to the patient daily, but at different intervals so that each was assimilated separately. In this way the patient received the same substances, except that they were not allowed to act upon each other. These patients showed little or no reticulocyte rise after feeding, thereby establishing the fact that the interaction of these substances whether *in vivo* or *in vitro*, is necessary to bring about improvement in the blood picture of the patients. The *in vitro* experiments effectively ruled out any possible effect of a secretion from normal gastric cells reaching the pernicious anæmia patient by way of the normal gastric juice, as this secretion by itself was impotent. The third series of experiments showed that the good results of this combination was not due to a summation of the effect of the two substances but to the interaction of the two, because no results followed the feeding of the incubated gastric juice and the meat when these two were given at separate intervals of time during the one day.

The authors therefore suggest the theory that the significant defect in the patient with pernicious anæmia is an inability to carry out some essential step in gastric digestion possibly protein splitting), thus causing a lack of whatever substance is successfully derived by the stomach of the normal individual from his food. A relationship is thus established between the stomach and the function of the bone marrow, and pernicious anæmia is relegated by these authors to the ever-growing group of dietary deficiency diseases.

E. S. MILLS

**Bronchiectasie et tuberculose. (Bronchiectasis and tuberculosis.)** Bernard, L., *Paris méd.* **19**: 257, Sept. 28, 1929.

Bernard states that the relationship between bronchiectasis and tuberculosis is not well understood. After refering to the classical anatomical forms of bronchiectasis, the cylindrical, ampullar, and beaded, he goes on to discuss the common symptoms of the disease, and the valuable aid given by x-ray examination after the injection of lipiodol. Repeated hæmoptysis in a person who is otherwise apparently in good health should arouse the suspicion of a previously latent tuberculosis or bronchiectasis. Chronic fibrous induration of the lung parenchyma may, of course, occur in

both affections. The diagnosis is to be made, as in three cases he reports, by the demonstration of the tubercle bacillus in the sputum. In these cases there is, of course, the efflorescence of tuberculosis on a bronchiectatic background. An important point in the diagnosis is the sudden change in the clinical picture. New signs appear—loss of weight, sweats, continued fever, and there may be a change in the roentgenological picture. Tuberculosis here is not the cause of the bronchiectasis, but a late complication, and, as such, exceptional. Syphilis can be excluded by the lack of any signs pointing to it. The author recognizes three categories of bronchiectasis due to tuberculosis —the dilatations with chronic ulcerative tuberculosis: (1) the ulcero-fibrous form; (2) the dilatations following acute and subacute tuberculosis; and (3) the chronic diffuse forms, the most frequent. Finally, the author points out that there are cases in which the specific bacilli are not found.

A. G. NICHOLLS

**Lead Poisoning from Snuff.** Reitzel, R. J., *Ann. Int. Med.* **3**: 378, Oct. 1929.

It is well known that snuff may be a source of lead poisoning. This was first pointed out by Model in 1784. Dr. Reitzel has found references to about 40 cases of lead poisoning from snuff since that time, and now adds four from his own experience.

Apparently there are three possible reasons for lead being present in snuff. (1) There may be adulteration in manufacture; (2) the wrappers may contain lead; (3) the spray used as an insecticide in the cultivation of the plant not infrequently contains lead arsenate.

The adulteration is done by adding lead oxide and chromate to increase the bulk and make the snuff a lighter colour. There is no adequate legislation to prevent this practice. Snuff is frequently wrapped in lead-foil and packed in lead-tin boxes, and when it is damp or contains acetic acid, both of which conditions may obtain, absorption of the lead from the wrapper is possible.

Dr. Reitzel's cases were all in middle-aged women, each of whom used a brand of snuff which was shown to contain 0.35 per cent of lead chromate, or 0.224 per cent of lead. In each case the fæces and urine were found to contain lead. One patient was free from symptoms for about a year after stopping the snuff. Another, soon after entering the hospital, died from an inoperable carcinoma of the cervix. She had been taking snuff for twenty years. Opportunity was taken to examine her organs for lead, and it was detected in both the liver and heart muscle in large amounts. It was particularly interesting that the carcinomatous growth also contained lead, and in much larger proportions than the other tissues, a point requiring further investigation. The third case was still in hospital, complaining of weakness, abdominal cramps, and pains in the limbs.

The fourth patient, when first seen in hospital, had been having increasing weakness and epigastric pains, with vomiting and loss of weight. She had been addicted to snuff for thirty-five years, and in the last eight months had had a habit of keeping it under her lip both day and night and swallowing the saliva. Apparently she used up an 8-oz. jar of snuff twice a week. As in the other cases the snuff was found to contain 0.2 per cent of lead, and it was detected also in the urine and fæces. The snuff was taken away and she made some improvement and left the hospital. In about two months she returned showing great weakness. She had taken to snuff again, and with this her appetite had failed, and nausea and vomiting had set in. The chief changes were related to deterioration of the nervous system generally, with myositis. She eventually died and a detailed post-mortem was performed, but nothing distinctive of plumbism was found.

H. E. MACDERMOT

**The Prophylactic Action of Ultra-Violet Rays in Rickets** Huldschinsky, K., *Brit. J. Actinother. & Physiother.* **4**: 185, Dec. 1929.

Rickets usually begins in the third month of life, and first evidences of it are rarely seen in children who have passed the age of one year. The most severe manifestations are not commonly observed before the fifth month. Prophylactic irradiation need not be instituted before the third month. In Huldschinsky's experience, one month of treatment had lasting prophylactic value only in children who had shown no signs of rickets, while two months' treatment did not always prevent further manifestations in cases in which signs were present before treatment was commenced. "Prophylaxis, in the sense we know it in protective inoculations, does not exist for rickets." The term must be interpreted rather to mean the cure of rickets before it has become clinically evident.

Three causal factors must be considered: (a) constitutional predisposition; (b) growth; (c) light deficiency. A constitutional factor must be recognized—an inherited predisposition or a congenital deficiency in protective materials. Only the growing organism is attacked by rickets, and those bones are affected most in which growth is most rapid—the cranial bones in the first six-month period, the ribs in the second, the extremities in the third. Growth may be considered the basic factor, as in most cases its association with either of the others will produce rickets. Overfeeding may prove provocative in a predisposed child. All three

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factors must be present to bring about the severe form of rickets.

There is a greater tendency to relapse in rickets than has been generally supposed, and this must be taken into account in the use of the ultra-violet rays. Treatment must be prolonged until all fear of danger from constitutional predisposition or climatic conditions is past. Irradiation must be extended over the "dark" period of the year and continued until all clinical symptoms have disappeared. It must be resumed "at the reappearance of the dark season as well as at the beginning of a new period of growth, *e.g.*, after completion of the first year of life."

The cure of rickets may result from one or two months of intensive treatment, but prophylactic treatment must be extended throughout the winter months and into at least the middle of the second year of the child's life. Prophylactic doses of the ultra-violet rays are much less than those required in therapy—generally a tenth part of the therapeutic dose suffices. Even winter sunlight has some prophylactic value, and the exposure of the face only to the winter sun of Berlin, for several hours daily, gave Huldschinsky good results in some cases.

When irradiated ergosterol is used continuously for prophylactic purposes, the dose should be about a one-hundredth part of the curative dose. There is uncertainty of dosage in irradiated milk, etc., and the administration of even irradiated ergosterol should be entrusted only to conscientious and intelligent persons. Failure must be expected if dosage is insufficient, and over-dosage is not devoid of danger.

W. H. HATTIE

**The Control of Scarlet Fever.** Dick, G. F., and Dick, G. H., *Am. J. Dis. Child.* **38**: 905, Nov. 1929.

The Dicks discuss the present status of scarlet fever control and therapy on the basis of observations made during the last six years on 32,440 persons on whom skin tests were made, 11,584 susceptible persons who were immunized by their toxin, and 967 cases of scarlet fever treated with the therapeutic serum.

They describe an exact technique for the skin test and indicate the common errors in method and interpretation. Positive reactions are frequently read as negative through failure to observe them in a bright light not more than twenty-four hours after the injection. "The slightest flush, no matter how faint the color, constitutes a positive reaction, if it measures as much as 10 mm. in any diameter." Of 20,856 persons with spontaneously negative skin tests none contracted the disease after exposure. The intensity of the reaction to the skin test is proportional to the susceptibility of the subject.

General reactions after active immunization are to be expected in 10 per cent of cases. Five graduated doses of the toxin, beginning with 500 skin test doses and increasing to 100,000 skin test doses may be counted on to immunize completely 95 per cent of susceptible persons. "Retests made at intervals of one, two and three years indicate that more than 90 per cent of those immunized to the point of an entirely negative skin reaction retain their immunity. "Eleven thousand five hundred and eighty-four persons showing positive skin tests were actively immunized and did not contract the disease in institutions where scarlet fever was epidemic. Ricinoleated toxin has no protective value.

The administration of prophylactic doses of antitoxin to all contacts is not justified. The Dicks advise waiting for the development of symptoms and giving the therapeutic dose early, unless it is possible to make skin tests and nose and throat cultures to determine which of the contacts require antitoxin. They advise the use of antitoxin in all cases of scarlet fever, and believe it effects a marked reduction in the incidence and severity of the complications.

A. K. GEDDES

**The Relationship of Vitamin C to the Soundness of the Teeth.** Eddy, W. H., *Am. J. Pub. Health* **19**: 1309, Dec. 1929.

In an article which appeared in the *American Journal of Public Health* for December last, entitled "An Improvement in the Quantitative Assay of the Antiscurvy Vitamin (c)," Walter H. Eddy discusses approvingly the Höjer method of assay of this vitamin. Höjer maintains that sections of the teeth of laboratory animals reveal histological pictures characteristic of scurvy or its absence, and that the study of such sections permits of a more rapid assay of antiscorbutic values than the older method of Sherman. Eddy's experimental work is confirmatory of Höjer's contention. The concluding paragraph of Eddy's article is worth noting. "With all the attention that vitamin D is receiving as a bone former to-day, and by inference as affecting tooth formation, it is at least significant to find that the major tooth forming factor is quite a different vitamin, and of value to recognize this fact in applying dietary measures to tooth health."

W. H. HATTIE

**Value of Blood Amylase Estimations in the Diagnosis of Pancreatic Disease.** Elman, R., Arneson, N., Graham, E. A. *Arch. Surg.* **19**: 943, 1929.

Because of the difficulties in the clinical diagnosis of disease of the pancreas, methods of estimating pancreatic function have been intro-

duced. These are based on the quantitative estimation of amylase in the blood plasma, since it is almost conclusively proved that amylase is of pancreatic origin.

Two methods of quantitative estimation of amylase have previously been tried, both based on the diastatic action of amylase on starch. The first method depended on the end-point of complete hydrolysis of starch, as shown by the disappearance of the blue colour which it produces with iodine. The second method depended on the formation of sugar, which was estimated quantitatively by some method of copper reduction. Both methods proved unsatisfactory because they showed a great fluctuation in the normal amylase content.

The method introduced by the authors is based on the rate of elimination of the viscosity of starch solution by the action of amylase. It has the great advantage that the ferment action is estimated by the time required to effect a given change, rather than by the amount of change in a given time. The method is roughly as follows: Five c.c. of a 3 per cent starch solution and 0.4 c.c. of the oxalated plasma to be tested are placed in an Ostwald viscosimeter. The solution is allowed to drain by gravity through a capillary tube, the time of outflow through the tube being measured by means of a stop-watch. Readings are made every few minutes until there is a 20 per cent reduction in the outflow time. The results are expressed by the formula $A.V.=\frac{60}{T.V.}$, where A.V. represents amylase units, T the time in minutes from the mixture of plasma and starch solution till the outflow time is reduced 20 per cent, and V the volume of plasma used.

By this method the concentration of amylase in human plasma was determined in sixty cases. Uniform values (4.3 to 6.8 units) were found in 25 cases where the pancreas was subsequently demonstrated to be normal. Deviations from normal were found in 21 out of 23 cases where pancreatic disease was subsequently found at operation or post-mortem.

P. G. SILVER

## SURGERY

**Two Cases of Riedel's Chronic Thyroiditis.** Wingate, H. F., *Brit. J. Surg.* **17**: 264, Oct. 1929.

Both cases occurred in women 46 and 34 years of age respectively. The former gave the history of a lump in the neck for six years, which in the last three months had increased rapidly in size. She complained of slight dyspnœa, occasional hoarseness, occasional palpitation, and of tiring easily. No evidence of tuberculosis could be made out. The Wassermann test was negative. The pulse rate was 80. The firmness of the gland raised the question of malignancy. At operation the right lobe and the isthmus were removed. There were adhesions to surrounding structures. A thickened capsule was present. The cut surface was finely lobulated, opaque, solid looking, and seemed devoid of colloid.

Two and one-half years after operation the patient was receiving thyroid extract. The left lobe gradually decreased in size. Microscopically, the capsule and interlobular septa were infiltrated with mononuclear cells; vessels were scanty; and some parts showed a hyaline stroma enclosing a few cells and no acini. Other areas showed very cellular granulomata with a minimal amount of stroma, plus great numbers of plasma cells, lymphocytes, and a few fibroblasts; considerable numbers of acini were present in some of these areas; a few acini had a small amount of colloid. Phagocytosis of epithelial cells by leucocytes or plasma cells was sometimes seen by high power. Definite lymph follicles, variable in size and shape, were present in all sections. Irregular hyaline material was seen among the cells. Many giant-cells were present under low power; they had no relation to the lymph follicles. Under the high power many of these cells were found to be masses of colloid invaded by phagocytes, often intra-acinar. The real giant-cells were foreign-body cells.

The second patient had had a swelling for five years. For the past year she had had severe attacks of dyspnœa. The Wassermann test was negative. At operation the gland was adherent to surrounding structures. On cut section, the right lobe was an opaque white, studded with yellowish areas of colloid. The histological appearance was that described above, except for areas of comparatively normal acini. Some of these showed hyperplasia.

Lymph follicles present in Riedel's thyroiditis represent hyperplasia of the minute lymphatic nodes found in many organs. The true nature of the lesion is probably that of a non-tuberculous granuloma.

STUART D. GORDON

**Direct and Indirect Injury to the Recurrent Laryngeal Nerves During Thyroidectomy.** Dixon, C. F., *Ann. Surg.* **90**: 982, Dec. 1929.

One of the commonest complications of thyroidectomy is injury to one or both recurrent laryngeal nerves. This injury may occur at the inferior pole, along the lateral surface of the trachea, or at the crico-thyroid juncture where the nerve pierces the larynx. Section of the nerve results in permanent injury, as does ligaturing of the nerve. Removal of the ligature results in prolonged but not permanent impairment. Stretching of the nerve also results in temporary impairment. Œdema or hæmorrhage affects the nerve, or nerves, usually within forty-eight hours of

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operation. Recovery occurs within two weeks in this type of injury.

Injury may be avoided by leaving a small amount of thyroid tissue on the lateral wall of the trachea. Suturing increases the chance of injury to the nerve. It is important that the patient be allowed to talk following extirpation of a lobe in order that the presence or absence of a nerve lesion may be determined. If one nerve is injured permanently there is little or no post-operative trouble. Severe tracheitis, plus an unilateral injury, may result in respiratory embarrassment for two or three days. Œdema of the glottis, plus such an injury, causes a narrowed breathing space. Both cords will be in adduction, but the uninjured one will move laterally on inspiration.

The treatment of a case showing respiratory obstruction due to indirect nerve injury (œdema or hæmorrhage) consisted in the exhibition of oxygen by means of an oxygen tent, and the application of hot moist dressings to the wound. Tracheotomy may have to be done to relieve obstruction and cyanosis. The tube is removed when the cords move normally.

STUART D. GORDON

**Pleurolysis (Jacobäus) and Oleothorax.** Häberlin, F., *J. State Med.* **37**: 12, 731, Dec. 1929.

In this paper Häberlin deals briefly with his own experience with the endoscopic pleurolysis introduced by Jacobäus, and the method of filling the pneumothorax cavity with oil introduced by Kûss and Bernou. Häberlin is the medical superintendent of a sanatorium situated near Davos. He opposes the practice of forcibly stretching or tearing adhesions by causing sudden rise of intrapleural pressure by means of the pneumothorax operation, as the site of the tear cannot be chosen. If a carefully administered pneumothorax does not show satisfactory results within three months, or if urgent indications for further intervention arise, such as hæmorrhage from an incompletely collapsed cavity, he advises pleurolysis.

A thoracoscope is used for inspection of the pleural cavity. This instrument is constructed like a small straight cystoscope, which fits tightly in a trocar. The trocar is inserted through an intercostal space, the mandrel withdrawn, and the endoscope introduced. Pressure with the finger on intercostal spaces often helps in demonstrating the location of adhesions. The sites of adhesions determine the point at which another trocar, to permit of electric cauterization, is to be inserted. If one insertion does not allow of severance by the cautery of all adhesions, change of position of the trocar is necessitated. It may be advisable to defer this for some days.

Marked clinical improvement and radiographs show the advantages of this operation. There are risks, of course. The principal things to fear are hæmorrhage and empyema. If the cautery is at red heat only there is little danger of hæmorrhage. Empyema may follow rupture of a cavity in the absence of failure in operative technique. Usually a small aseptic exudate follows the operation, but this disappears in a few days. Häberlin maintains that the benefit and risk are greatly in favour of this operation, and that in the case of an unsatisfactory pneumothorax it should be employed before recourse to other methods of collapse therapy.

Just as the good results which were noted after spontaneous pneumothorax suggested artificial pneumothorax, so the results which follow upon an exudate induced by the pneumothorax operation have suggested the introduction of oil to the pleural cavity in case Nature does not supply sufficient exudate to compress cavities and enforce healing. Except in those in which there had been no previous exudate, which reacted with an aseptic effusion and a moderate fever lasting for from a few days to several weeks, no untoward results followed in the cases reported by Häberlin. The ultimate result in the cases which reacted was gratifying. Oil-filling was resorted to, with good results, in several patients who could not report regularly for pneumothorax refills, and in one patient with tuberculous empyema.

W. H. HATTIE

## OBSTETRICS AND GYNÆCOLOGY

**An Unusual Vaginal Infection in a Young Married Woman.** Wordley, E., *The Lancet* **2**: 1035, Nov. 16, 1929.

A case is reported to show with what ease an erroneous diagnosis may be made in suspecting venereal infection.

A woman, aged 20, eight days after a runaway marriage, noted profuse vaginal discharge with irritation about the vulva. The physical signs suggested gonorrhœa and smears showed pus cells with numerous Gram-negative diplococci, intra- and extra-cellular. In view of prospective divorce proceedings, further investigation was carried out. Repeated examination showed thick yellow discharge and much local tenderness as well as enlargement of the inguinal glands. Smears again demonstrated organisms indistinguishable from gonococci. Cultures were taken and the most notable observation was that the organism grew abundantly on plain agar at both 37 degrees and at room temperature. This growth at room temperature absolutely precluded the possibility of the organism being gonococcus.

On examination of the husband, there was no history or sign of infection and smears from the urethra, prostatic secretion, and the urine gave

no pus or bacteria. The wife's infection cleared up rapidly with simple douches. There was no possibility under the circumstances of the girl having been exposed to infection except from the husband, and it was learned that a great deal of pain followed the first coitus. It is thought that this trauma started an infection with *M. catarrhalis* or some allied organism, but the exact imitation of a gonorrhœal infection, and the disastrous results of such a diagnosis, are apparent and instructive.

J. B. ROSS

## PÆDIATRICS

**Tonsillectomy in the Prevention and Treatment of Rheumatism.** Findlay, L., MacFarlane, J. W., and Stevenson, M. M., *Arch. Dis. Child.* **4**: 313, Oct. 1929.

One hundred and fifty-three rheumatic children in Glasgow, followed for a period of five to eight years and tonsillectomized for the most part at the mid-point of this period of observation, constitute the material for this analytical survey. The authors' summary is as follows:

1. A preliminary tonsillectomy may possibly render an individual less susceptible to rheumatic arthritis but not to chorea.

2. A preliminary tonsillectomy, or one performed early during the course of the infection, may possibly, in the case of arthritis, render the heart less liable to be attacked, but not so in the case of chorea.

3. As, however, cardiac complications usually ensue during the first or second rheumatic manifestations the operation to be prophylactic must be performed before the second attack.

4. Tonsillectomy in the case of carditis following arthritis seems to have a beneficial effect on the progress of the disease, but not so in carditis following chorea.

5. The evidence in favour of the above beneficial effect of tonsillectomy in the case of rheumatic manifestations characterized by arthritis is, however, very slight.

6. The varying behaviour in response to tonsillectomy of examples of the rheumatic infection characterized by chorea and by arthritis suggests the possibility of a different strain of the infective agent in these two types of the disease.

A. K. GEDDES

**Effect of Tonsillectomy and of Adenoidectomy on Diphtheria Immunity.** Schick, B., and Topper, A., *Am. J. Dis. Child.* **38**: 929, Nov. 1929.

Statements of many clinicians are cited as to the rarity of diphtheria in children who have had their tonsils removed. Over a period of three years a Schick test was made on all children coming to the Mount Sinai Hospital in New York for tonsillectomy, and all positive reactors were re-tested six months after the tonsillectomy. One hundred children between two and twelve years of age were thus followed; 61 were between two and six years old and 39 were between six and twelve. Six months after tonsillectomy 18 per cent of these were still positive and in 82 per cent the reaction had become negative. Comparison of these data with the statistics of Park, Zingher, and others on normal susceptibility to diphtheria shows that such a high rate of immunity does not ordinarily develop until adult life.

Of 340 consecutive admissions (for all diseases) of children between two and thirteen years of age, 200 had had their tonsils removed. Schick tests made on this tonsillectomized group gave positive reactions in 19 per cent and negative in 81 per cent.

This study demonstrates that in a large proportion of children a definite immunity to diphtheria is developed after tonsillectomy; that this acquired protection is a humoral immunity, rather than a local mechanism due to the eradication of tissue specially favourable for the growth of the diphtheria bacillus. The authors discuss the possible mechanisms of the development of this immunity. They recommended that children who have been tonsillectomized six months or more previously be Schick-tested before being immunized against diphtheria.

A. K. GEDDES

**Studies of Pneumonia in Childhood: No. V. Empyema.** McNeil, C., Macgregor, A. R., and Alexander, W. A., *Arch. Dis. Child.* **4**: 270, Oct. 1929.

This is the final paper of a series of five clinical and pathological studies of pneumonia and its complications, on a basis of 648 cases of pneumonia and 244 autopsies. In studying the pathology large thin sections of the entire lung were used. All the articles are beautifully illustrated.

In the clinical series of 648 cases of pneumonia in children from birth to twelve years, empyema occurred in one case out of every seven. The death rate in this empyema series was 40 per cent; in the age period from birth to two years it was 75 per cent. The mortality was much higher in those cases with a coexistent pneumonia than in the metapneumonic cases.

In the pathological series of 244 cases of pneumonia, 27 per cent were complicated by empyema. In most of these empyema cases some pneumonia was present at the time of death. One-half of the empyemata occurred in cases of bronchopneumonia. Thirty per cent were associated with other complications of pneumonia-pericarditis, peritonitis and meningitis. One-half the cases of bronchopneumonia

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with empyema showed lung abscess. Fibrosis of the lung was common.

A. K. GEDDES

**The Prognosis of Acute Nephritis in Childhood.** Lyttle, J. D., and Rosenberg, L., *Am. J. Dis. Child.* **38**: 1052, Nov. 1929.

The 99 cases of acute nephritis analyzed in this article were classified as acute glomerular, 74; acute diffuse (glomerulo-tubular), 17; acute tubular, 8. In the great majority of cases, tubular as well as glomerular, the onset was preceded by a respiratory infection. Scarlet fever was rare as a causative agent. The mortality rate for the series was 11 per cent: by subgroups; acute glomerular, 5 per cent; acute diffuse, 12 per cent; tubular, 62 per cent.

Fifteen per cent of the cases followed became chronic. By subgroups, 5 per cent of the glomerular, 18 per cent of the diffuse, and 25 per cent of the tubular became chronic. Most of these patients had a chronic or persistent infection, or repeated acute infections of the respiratory tract, middle ear, or sinuses. The degree of œdema, hæmaturia, hypertension, and nitrogen retention, while influencing the acute attack, had little relation to chronicity. Mild attacks of acute nephritis progressed to chronic nephritis as frequently as did severe attacks. Cases with uræmia had a high mortality, but showed no increased tendency to chronicity.

The authors compare their figures with the statistics of other series in the literature. They believe that the determining factor in the development of chronic nephritis is persistent or recurrent infection.

A. K. GEDDES

## THERAPEUTICS

**The Present Status of Convalescent Serum Therapy.** Kellogg, W. H., *J. Am. M. Ass.* **93**: 1927, Dec. 21, 1929.

Dr. Kellogg considers that the use of convalescent serum has been proved satisfactory in measles and poliomyelitis only. In measles it has preventive powers, but is useless as a cure once the disease is established. The passive immunity produced may be only partial but at least the attack will be mild and uncomplicated. In poliomyelitis the situation is not so clear. Those who publish their own results naturally put things in the most favourable light; adequate controls are very hard to obtain. Acute anterior poliomyelitis is breaking out in epidemic form more frequently, so that this problem is a very pressing one.

The experimental work has been done on monkeys, and convalescent serum has been proved to have certain powers. It protects monkeys from inoculation and makes the virus ineffective if mixed with it before inoculation. The portal of entry has been shown to be the nasal mucous membrane and the lymph channels of the olfactory nerves. The choroid plexus is the barrier to the meninges and what agency breaks it down is uncertain. For this reason it seems illogical to introduce serum into the vertebral canal unless it is virucidal. Normal horse serum was used in this way and apparently was curative, which raises the question—Is the serum virucidal, or have we merely the effect of a foreign protein?

The value of reports of cases treated with serum is difficult to ascertain for several reasons; the difference in severity at different periods of an epidemic; the difficulty in getting an unbiased selection of cases; the inaccuracy of diagnosis; and the fact that the infection is always present before serum is given. Dr. Kellogg quotes the figures of two extensive reports, one from Winnipeg, but feels that there are gaps in the chain of evidence in both reports. There seems no doubt that the serum should be given intraspinally, and that the danger of spinal puncture can be disregarded. Several reported that early drainage of the spinal fluid seemed to help.

The author's conclusion is that convalescent serum given in the early stages of poliomyelitis is effective when given intrathecally, but that further study with more care in diagnosis and recording of cases and controls is necessary.

P. M. MACDONNELL

**The Influence of Liver Treatment on the Mortality from Pernicious Anæmia.** McKinley, P. L., *The Lancet* **2**: 1086, Nov. 23, 1929.

A statistical review of the mortality rates from pernicious anæmia in England and Wales is made with an effort to appraise the effect of the dietary method of treatment. The figures are taken from the records of 1921 to 1928 inclusive, and this period is subdivided into two parts —that of 1921 to 1926, before liver therapy was introduced, and that of 1927 to 1928, under the Minot-Murphy régime. It is found that the first group shows a practically level course of mortality rate without significant variation. In 1927 there was a slight evidence of improvement in the death rate in males, this only rising to the level of importance in the last three months of the year. In 1928, however, there is a marked improvement affecting both sexes, chiefly the young adult and middle ages, and progressing steadily in importance to the end of the year. The total gain was some 915 deaths less than expectancy. The fact that the change is notable first in the statistics of London and the larger centres and increases as the year goes on, in the absence of any factor other than diet, strongly suggests that the change in the death rate is closely dependent on the introduction and spread of this method

of therapy. The evidence is consistent with a causal relation between the two occurrences, and there is every reason to predict that an extension of the treatment to wider limits will be followed by a further and more widespread reduction in mortality figures from this disease.

J. B. ROSS

**Preparation of Dextrose for Intraperitoneal Injection.** Shohl, A. T., and Beal, F., *Am. J. Dis. Child.* **38**: 943, Nov. 1929.

A method of preparing dextrose for intraperitoneal injection is described. A test-tube containing the required amount of dextrose is stoppered with cotton and inverted in a wide-mouthed bottle containing 25 to 30 grams of anhydrous calcium chloride as a dessicating agent, and autoclaved for twenty minutes at 15 pounds pressure. Freshly distilled water is added to the dextrose and the solution is ready for use.

A. K. GEDDES

## PATHOLOGY

**Idiopathische diffuse Œsophagushypertrophie. (Idiopathic diffuse hypertrophy of the œsophagus.)** Goedel, A., *Wiener med. Wchnsch.* **42**: 1009, 1929.

The author reports, from the Empress Elizabeth Hospital in Vienna, a curious case of diffuse idiopathic hypertrophy of the œsophagus, which was found in a patient who had died of sepsis. The œsophagus was extraordinarily thickened, being converted into a stiff elongated tube, which measured externally seven cm. in circumference, while the lumen was only one cm. in diameter. The hypertrophy was found to be located in the muscular part of the wall, and chiefly in the circular fibres. Microscopically, no evidences of recent or old inflammation could be detected. Curiously, the patient in question had never manifested any symptoms of spasm of the œsophagus of a functional character. All the other cases on record have been of the same kind, that is, devoid of clinical symptoms during life, and the condition of the œsophagus has been an unexpected finding in the course of autopsy.

A. G. NICHOLLS

## HYGIENE AND PUBLIC HEALTH

**The Tuberculosis League, the Sanatorium and Industry.** Coleman, B. S., *J. Industr. Hygiene* **11**: 217, September, 1929.

Within the past few years it has been fully recognized that tuberculosis is essentially a problem of the working man and woman, since one out of every four deaths between the ages of 15 and 45 occurs from that disease. Coupled with this has been the realization that the most valuable approach we have to the great mass of tuberculous adults is through medical service in industry. Credit for the start in this work is to be given to the Philadelphia Health Council and Tuberculosis Committee, following Dr. Horwood's Tuberculosis Survey of that city in 1922. In 1928, after this lead, the Hudson County (N.J.) Tuberculosis League inaugurated its industrial health service.

The League began work by an intensive educational campaign of interviews with employers, noon time talks to employees, and the distribution of posters, leaflets and pamphlets on health matters; in all these the value of health examinations was stressed. After the consent of the employers and employees was obtained the examination teams of doctors and nurses were set to work at the various plants at typical periodical health examinations. The usual number of minor defects of teeth, tonsils, nutrition, posture and habits was found. Letters summarizing the findings in each case were sent to the employees' houses, advising consultation with the family physician or with clinics. Nurses, detailed to follow up, got in touch with the employee, the family physician or the clinic, as the case might be.

The Hudson County Tuberculosis Clinics which are open daily and one night a week were found very valuable in follow-up and x-ray work of suspected cases. Should the bread winner of the family be required to go to sanatorium the State Board of Children's Guardians' Fund looks after the children.

It is interesting to note that among 3,500 employees examined in the city of Newark, eighty positive and observation cases of tuberculosis were found, of which 60 were later definitely diagnosed as tuberculosis and 39 were sent to sanatoria.

Later, as the value of health supervision becomes more apparent to employers, it is hoped to transfer the burden of these health services to the industries—the larger ones to employ a physician and nurse and the smaller ones to join into groups of 1,000 employees sharing a unit health service of pre-employment examination, routine physical examinations, first aid treatments of minor illness and injury, and health education.

So much for a scheme whereby those who need sanatorium care are discovered early in industry. When the employee is discharged from care the closest co-operation between the sanatorium and the industry is once more necessary in order that the man may be placed in the best possible environment to maintain his newly gained health. Three months before his discharge a patient should be given carefully supervised employment about the sanatorium:

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the physician in charge should notify the industry from which he came of his impending release and submit a careful evaluation of his ability to work.

Many county health leagues are now maintaining replacement and rehabilitation bureaus to obtain suitable positions for those discharged from sanatorium care.

As a general rule a tuberculous person should return to the work for which his previous experience fits him. The training of adults more than twenty-five years of age in a new occupation is not practicable as a general policy.

N. VANCE WARD

**Health and Scholastic Attainments.** Diehl, H. S., *Public Health Reports* **44**: 3041, Dec. 13, 1929.

This study comes from the University of Minnesota Student's Health Service and compares the physique, habits of living, the social and academic status of 141 university students who were on probation because of poor scholarship with the condition of 496 students doing satisfactory work. It might be supposed that physical energy with indulgence in recreation would be a factor in contributing to poor scholarship. On this basis one might expect a group of failures to compare favourably with respect to physique with a group of successful college students. This study does not support this theory, and the students on probation, on the average, compare unfavourably with the successful group. Conditions of overweight and underweight, bad posture and anæmia were found to predominate significantly in the probationary group. Students who were partially self-supporting occurred on the average in greater numbers in the successful group than in the probationary group, but the reverse was true of students who were entirely self-supporting.

Results of this study are in line with studies of school children which have shown a positive correlation between mental development and physical growth.

FRANK G. PEDLEY

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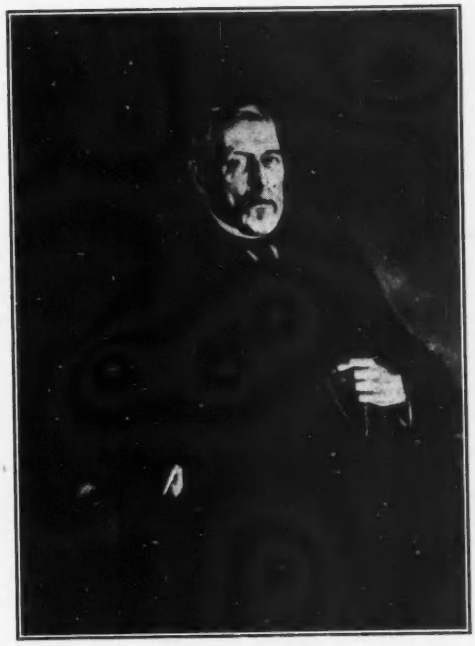
AJINOMOTO.—Whenever protein is eaten, it is hydrolyzed by the digestive juices and a mixture of some twenty aminoacids is produced and subsequently absorbed. In spite of the fact that this is a familiar biochemical reaction so common as to excite little notice, the laboratory production of pure crystalline amino-acids is accomplished only with difficulty, so that these compounds are listed as rare chemicals and are usually found only in research laboratories. Recently attention has been called again to the fact that the acid sodium salt of glutamic acid, an amino-acid occurring in proteins, is made in large quantities for food purposes in the orient. It was discovered in Japan that this salt has a decided meatlike taste. The use of meat in the diet is condemned by Buddhists and, instead, shavings of dried fish were added to many of the Japanese dishes to improve the flavour. With the advent of monosodium glutamate in commerce, this condiment is said to have become as common in Japanese cookery as was salt or sugar. It is called "Ajinomoto," or "the element of taste." The Chinese have become large users of this material, the great number of vegetarians among them creating a demand for it. This condiment has also been used to displace the more expensive chicken and meat extract formerly used to impart taste to their dishes. Monosodium glutamate is made by hydrolyzing gluten or soy bean by hydrochloric or sulphuric acid. The manufacture began in China about eight years ago and Han states that the value of this chemical made in China in 1928 was $630,000 and that $500,000 worth more was imported from Japan. The export of this material from China to the Philippines, Dutch East Indies and Singapore has become a trade of considerable magnitude. While the cost of glutamic acid in this country is about $15 for 100 Gm., the price of Ajinomoto is from $2 to $3 a pound. The exigencies of religion, of racial food habits and of economics have transformed what in this country is a rare chemical to a common article of food among the oriental nations.—*J. Am. M. Ass.*, Nov. 30, 1929.

UNDULANT FEVER IN THE UNITED STATES.—The organism which causes contagious abortion in cows causes undulant fever in man. According to the Bureau of Animal Industry of the United States Department of Agriculture, contagious abortion in cattle has greatly increased and in many regions 35 per cent, or even more, of the herds are infected. Raw milk from these herds is dangerous to human beings. In 1928 there were recorded five hundred and sixty positive cases of undulant fever distributed over forty states. The largest number of these cases, one hundred and eighteen, was reported by Iowa; New York reported forty-five cases; Indiana, forty cases; and Michigan, thirty-four cases. During the same year, there were, in the United States and Canada, forty milk-borne epidemics of other diseases and three epidemics of undulant fever. These forty-three epidemics involved twenty-one hundred and twenty-nine cases and caused ninety-four deaths. Undulant fever in epidemic form was first reported in the United States in 1922, from Phoenix, Arizona. It is only within the last few years, however, that State Health Departments have undertaken the diagnosis of undulant fever in man by routine examination of samples of blood. Indeed many states began to make these tests as late as 1928. Undulant fever is a lingering illness that weakens and incapacitates its victims over a long period of time, even of years. Therefore, it is not a disease to be considered lightly. Since the source of the contagion is milk, the disease can be prevented by rendering the milk supply clean and safe. There is unanimity of proof that pasteurization at the standard temperatures is completely effective so far as the organism causing undulant fever is concerned. With each new advance in the knowledge of infectious diseases, we are impressed with what appears to be the increasing health hazard in relation to those diseases due to the consumption of raw milk.

# Obituaries

**Dr. Murdoch Chisholm,** one of the oldest and most respected of the medical profession in the Maritime Provinces, and a Past-President of the Canadian Medical Association, died at Halifax, N.S., on December 29, 1929.

Dr. Chisholm was born at Loch Lomond, Cape Breton, in 1848. After taking part of the Arts Course at Dalhousie University, he entered on the study of medicine at McGill, receiving the degrees of M.D., C.M., in 1879. He was the oldest graduate in medicine of McGill University in the Maritimes. Some time later Dr. Chisholm proceeded to London for post-graduate study, where he obtained the diploma of L.R.C.P. in 1886.



Dr. Murdoch Chisholm

Dr. Chisholm was early identified with medical teaching in Halifax, becoming successively Professor of Clinical Medicine (1891), Professor of Clinical Surgery (1897), and Professor of Surgery and Clinical Surgery (1898) in the old Halifax Medical College. He retired as Professor of Surgery in 1910, retaining the clinical Chair until 1911, when the institution was merged into the newly constituted Faculty of Medicine of Dalhousie University. Dr. Chisholm continued to hold the same position in the University until 1923, when he retired with the rank of Emeritus Professor. He received the degree of LL.D., *honoris causa*, from Dalhousie University in 1919. For many years Dr. Chisholm was on the staff of the Victoria General Hospital, Halifax.

### An Appreciation

A little more than two months ago we celebrated the professional jubilee of Dr. Murdoch Chisholm. We told him then, as we had often done before, that we loved him. It was really quite unnecessary. He knew nothing but love for his fellows; why should he have expected anything but love in return? We had previously honoured him as we could. He had been president of our local society, of our provincial society, of the now extinct maritime association, and of the national association. He had had many evidences of our esteem. And yet he was pleased when we made his completion of a half century of medical practice the occasion for reaffirming our affection for him. Now that he has bade us farewell, we are glad that we gave him that pleasure, and among the many beautiful memories we will hold of him will be that of the modest, unaffected way in which he received our tributes on that memorable evening.

It can be said in all sincerity that Murdoch Chisholm was a very exceptional character. His diagnostic acumen was almost weird. He was singularly successful in his surgical work, conservative, and resourceful, and his ingenuity in overcoming difficulties brought many a thrill to onlookers in the operating room. He was in much demand as a consultant in purely medical cases. As a teacher he won the heart of every student by his sincerity, his originality of expression, his kindly humour, his clarity of thought, and his ready response to every request for further explanation. He made no parade of his knowledge, but no one could be with him long without being impressed with the catholicity of his interests and the keenness of his reasoning. He wrote frequently to the lay press, discussing such diverse problems as politics and religion, travel and prohibition. He could show impatience with what he regarded as heresy or bigotry, but he could not be unkind. Tales are told of such complete absorption in some abstruse problem that appointments were forgotten, and of occasions when his horse stood waiting in front of a patient's house while he walked home. No man could have had more delightful eccentricities. But the quality which impressed everyone he met was his friendliness. Nothing could have been more genuine or more unaffected, and it inevitably brought immediate response alike from rich and poor, learned and unlearned. Has anyone ever heard an unkind work spoken of him?

As might be expected, Dr. Chisholm held strong religious convictions. He was a devout student of The Book, and wrote two small volumes in which he set forth his theological views with characteristic frankness. Modernists in religious thought made small appeal to him, and he was generally critical of their attitude, but he could not be accused of intolerance.

Dr. Chisholm carried on in spite of a heavy handicap. He suffered much from asthma, and often operated when in evident distress. But even when the attacks were most severe, his serenity was undisturbed and his alertness was undiminished. Fortunately this handicap was considerably reduced some years ago, when the introduction of sensitivity tests discovered means of rendering attacks much less frequent.

A few years after graduation at McGill, Dr. Chisholm took up graduate work in England and elsewhere, and obtained the license of the Royal College of Physicians. He was a frequent visitor to medical centres on both sides of the Atlantic, and occasionally indulged himself in travel for the love he had for it. Dalhousie, noted for its parsimony in granting honorary degrees, made him an LL.D. The North British Society of Halifax, most ancient of our societies, elected him to its presidency. He served terms in the Halifax city council and as chairman of the City Health Board. For many years he was on the staff of the Victoria General Hospital, and gave his services freely to a number of institutions in the city; and he was a tower of strength to the old Halifax Medical College, and to the medical school of Dalhousie Uni-

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versity. His was indeed a busy life, devoted with singular unselfishness to the benefit of his fellows.

When Murdoch Chisholm died, on the twenty-ninth of December, all Halifax, and indeed all Nova Scotia, mourned the passing of a great and good man who throughout a long life and until within a few days of his death went about doing good.

W. H. HATTIE

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**Dr. Naboth Allen,** of Vancouver, B.C., died unexpectedly in the Vancouver General Hospital on December 28, 1929, at the age of 58.

The late Dr. Allen was born in Greenspond, Newfoundland, and at the age of nineteen migrated to British Columbia. After spending several years in Vancouver and Victoria, the spirit of adventure drew him to Behring Sea on a sealing expedition. The next few years of his life were spent in Alaskan and Siberian waters. Later, he decided to enter the medical profession, and in 1903 received his degree in San Francisco. Returning to Vancouver, the next twenty-six years of his life were devoted to the practice of his profession. After spending some time at the Rotunda Hospital in Dublin, Dr. Allen's interests lay mainly in the field of obstetrics.

He is survived by his wife; his mother in St. John's, Newfoundland; one daughter and three sons in Vancouver.

The funeral, which took place on December 30th, was attended by the majority of the medical profession of Vancouver.

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**Dr. Paul. Parker Balcom,** of Berwick, Nova Scotia, died on December 19, 1929, after a short illness. Dr. Balcom graduated in 1915, and for some time thereafter was associated with his father, the late Dr. P. N. Balcom, of Aylesford, who was for many years a prominent member of the Nova Scotia profession. After his removal to Berwick, the "young Dr. Balcom" soon became established in a large practice and identified himself with several non-medical activities. His death was due to pneumonia.

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**Dr. L. A. Beaudry.** After a long illness Dr. L. A. Beaudry, who had practised in St. Hyacinthe, Que., for the last forty years, died at his home, on December 21st. He was 66 years of age.

The deceased was born in St. Hyacinthe, on August 14, 1863; he studied at the St. Hyacinthe Seminary, received his degree from the Royal Medical College at Montreal and practised in St. Hyacinthe all his life.

Dr. Beaudry is survived by two brothers: Paul Beaudry, K.C., of Montreal, and Laurent Beaudry, former secretary of the Canadian Embassy at Washington and at present Councillor in the Department of the Exterior at Ottawa, and two sisters Mrs. C. A. Archambault, of Montreal, and Emilie, of St. Hyacinthe.

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**Dr. Wm. Deinstadt,** of St. Stephen, N.B., died in Vancouver on November 28th. His body was brought to St. Stephen and was buried there on December 6th. Dr. Deinstadt was a native of Nova Scotia and at his death was in his 82nd year. He graduated in medicine from Harvard Medical School, coming to St. Stephen in 1876. Lately, due to advanced years, Dr. Deinstadt removed to Vancouver, where he lived with his daughter. He enjoyed an exceptionally large practice during his long residence in St. Stephen and was the beloved family physician of many of the older families of the community. Dr. Deinstadt always took much interest in the civic government of his home town, especially in the matter of schools.

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**Dr. D. V. Landry,** District Medical Health Officer for the Provincial Department of Health, died suddenly at Bathurst, N.B., on December 18th, while attending a meeting of the local Board of Health. Dr. Landry had a most notable career in provincial politics, serving as a member of the cabinet under four premiers. He was an orator of exceptional gifts and a fluent speaker of both French and English. Dr. Landry was born in Memramcook in 1866, the son of Vital J. Landry and his wife, Matilda D. Cormier. He was educated at St. Joseph's University, Memramcook. In March, 1927, Dr. Landry was appointed Medical Health Officer for the newly created northern district and the value of his work may be estimated by an eulogy published in the local papers and signed by Dr. G. G. Melvin, the Chief of the Public Health Service.

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**Dr. John W. R. Richardson.** The death occurred in the Vancouver General Hospital on January 4, 1930, of Capt. John W. R. Richardson, O.B.E., M.C., F.R.C.P., F.R.C.S., late of the Royal Army Medical Corps, at the age of 52 years.

The late Dr. Richardson, who was born in England, was on a visit to British Columbia and was without immediate relatives in this province. The funeral service was held on January 11, 1930.

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**Dr. Siffroi Henri Thibault,** of Comeauville, Nova Scotia, died on December 17, 1929. After completing the Arts course at St. Mary's College, he began medical studies at Dalhousie, and graduated in 1911. Within a few years of graduation, pulmonary tuberculosis became evident, and it was necessary for him to restrict his activities, but, except for occasional periods of rest, he continued practice until some months ago. He was highly regarded in his constituency, where his death is sincerely mourned.

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POST-VACCINAL ENCEPHALITIS.—The European experience with post-vaccinal encephalitis is the subject of extended comment in the current *Annals of Internal Medicine*, which reflects the very general reluctance of American pathologists to believe that a pure vaccine virus can produce encephalitis. It is not long since Dr. Richard Thompson, of Columbia University (a Fellow in Medicine of the National Research Council), reported his failure to produce vaccinal encephalitis in rabbits with a testicular virus. With direct intracerebral injection attempts to adapt the virus by brain and brain passage, at seven day intervals, gave negative results. Alternating brain and testicular passage, as used originally by Levaditi, was no more successful. Thompson considered that a possible explanation of the discrepancy between his results and those of so many European workers might be in variations in the strain of virus employed; that some would produce encephalitis without difficulty, others only after adaptation, and still others not at all. He mentions also the theory of Camus that the vaccine virus may be contaminated by some unknown neurotropic virus. It is to this latter theory that the editorial above mentioned very definitely leans. May not the unknown virus be simply the normal virus of rabbit encephalitis carried over with rabbit lymph, and may it not produce encephalitis in susceptible human beings? Up to the present four cases of post-vaccinal encephalitis have been reported in the United States. It is urged that, until the question of the etiology of this disease is settled, the use of rabbit lymph in vaccination should be stopped.

# News Items

## GREAT BRITAIN

### The Radcliffe Infirmary, Oxford

The Radcliffe Infirmary at Oxford has for a long time felt the need for expansion. It has now acquired for the sum of £100,000, largely through the generosity of Sir William Morris, the land adjacent which is occupied at present by the Radcliffe Observatory. Additional buildings will be provided, including a much needed maternity block.

The name Radcliffe recalls one of the outstanding benefactors of Oxford. John Radcliffe was a poor boy who eventually made a great position for himself. Educated at Oxford, he became Fellow of Lincoln College, and the most noted English physician of his time. As President of the Royal College of Physicians he is one of those noticed in the famous "Gold-headed Cane" of MacMichael. He became very wealthy, and on his decease in 1729 bequeathed his whole fortune, some £140,000, to his alma mater. He is commemorated in Oxford by the Radcliffe Library, Infirmary, and Observatory.

Three centuries later, another benefactor of the university arose in Cecil Rhodes, who, with money made in South Africa, endowed the Rhodes Scholarships. As illustrating the curious changes that sometimes occur in the whirligig of time, it is announced that the Radcliffe Observatory is to be removed in due course to the central plateau of South Africa, where the conditions for astronomical observation are the best in the world.

### The 150th Anniversary of The General Hospital, Birmingham

The General Hospital in Birmingham was founded in 1779 through the efforts of Dr. John Ash, F.R.S., F.R.C.P., and a band of enthusiastic supporters. Owing to various difficulties which arose, the plan which was conceived in 1765 was only put into practical operation fourteen years later. Associated with Dr. Ash on the first medical staff was Dr. William Withering, celebrated as the man who first wrote upon the medical qualities of digitalis.

The commemoration proceedings were begun on September 29, 1929, the birthday of the institution, privately by the hospital staff. The more formal proceedings were postponed until December 10th when a special religious service was held in the Cathedral at midday and in the afternoon addresses were given by Prof. K. F. Wenckebach, F.R.C.P., of Vienna and Lord Moynihan, President of the Royal College of Surgeons. In the evening a banquet was held when Lord Moynihan, the Lord Mayor, Sir John Ross Bradford, Dr. Stanley Barnes and Professor Wenckebach spoke.

### The New Offices of The Lancet

Towards the end of October last year the editorial and publishing offices of *The Lancet* were transferred from 1 Bedford Street and 423 Strand to the delightful house known as 7, Adam Street, Adelphi, whose freehold has been purchased by the proprietors. The move is a short one, for the buildings are only a hundred yards apart. Throughout its long history the editorial office of the *Lancet* has been in or very near the Strand, and our contemporary, in changing its quarters, has been able to maintain an unbroken tradition. From its first issue in 1823 until 1847 the paper was edited from a house in Norfolk Street, where Thomas Wakley, the founder, was engaged in private practice. In 1847 Wakley acquired the lease of the familiar building at the corner of Bedford Street, and from that time until 1921 the printing office was on the same premises. No. 7, Adam Street, stands in the middle of the eastern boundary of the famous block of buildings erected on the north bank of the Thames by Robert Adam and his brothers, John, James, and William, their joint authorship appearing in the word Adelphi— *ἀδελφοί*. The construction upon vaulted arches of these symmetrical streets was begun in 1773. The names of the two younger brothers have disappeared from their streets, and the connecting passage between the Strand and the Adelphi, at the north-west corner of the quadrangle, is now named Durham-house Street, in commemoration of the fact that nearly the whole area was once occupied by the town house of the bishops of Durham.

### The Birth Place of Lord Lister

An appeal for the preservation of the house in which the famous surgeon was born has been issued over the signatures of the Bishops of Chelmsford and Barking, Lord Moynihan, and Sir James Slade, and with the support of Sir Humphry Rolleston, Sir William Lister, Sir StClair Thomson, and others.

Upton House, Plaistow, in Lister's childhood was a delightful Georgian mansion, situated in what was hardly more than a village. Now it is in a densely populated industrial district of London. Shorn of some of its rooms and stables, and of much of its garden, it still is in occupation as the vicarage of St. Peter's, Upton Cross.

The house was purchased by the St. Albans diocesan authorities in 1885 and would have been sold by them on account of its dilapidated condition in 1918 had not the present vicar, the Rev. A. J. Parry, intervened and himself paid for the necessary structural repairs. A sum of £1800 it is stated would now capitalise the estimated annual dilapidations and preserve the house as the vicarage of the benefice. Should more money be subscribed the surplus would be used for setting up some memorial of Lister in the house itself. Cheques may be drawn in favour of "Lord Lister's Birthplace Preservation Fund," and sent to the hon. treasurers of the Fund at Upton House, Forest Gate, London, E.7.

Upton House, it may be recalled, is thus described in Dr. H. H. Bashford's "The Harley Street Calendar" (London: Constable and Co. 1929), p. 209:—

"Shorn of a wing and most of its garden, and the whole of the fields in which it stood, it is now the vicarage of an industrial parish, long since enveloped by the East of London. But at Lister's birth it was one of a little group of gracious and prosperous early eighteenth-century houses, surrounded by the farmlands of Thames-side, Essex, with the wild fowl nesting in Barking Marshes, and the panelled bedroom in which he was born looking westwards over Ham Park. This was the home—now an 'open space' carefully protected by Corporation railings—of his father's friend and fellow quaker, the Lombard-street banker, Samuel Gurney. And before the coming of the railway, when Lister was twelve years old—the fourth child in a family of seven—Mr. Lister and his neighbours, when the weather was fine, rode to their offices on horseback, or were collected by a coach, waiting at convenient points, and signalling its arrival by a horn."

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### A Badge for the President's Lady

It was announced at a recent meeting of the Council of the British Medical Association that the President, Professor Burgess, had offered to present to the Association a badge to be worn by the President's lady at Association functions, the badge to be on somewhat similar lines to the Past-President's decoration. The President said that the idea arose out of a remark made casually at the Manchester meeting by Mrs. Harvey Smith, wife of the President-Elect. The offer of the President was accepted with applause, and the Chairman remarked that the first lady to wear it should certainly be Mrs. Burgess, and that occasion would be found for the ceremony of presentation at the Annual Representative Meeting.

## NOVA SCOTIA

The Digby Hospital Board have decided to proceed with the erection of a new hospital building, and to have the work done under the supervision of the Board rather than by contract.

More than fifty members of the original Dalhousie Unit (Seventh Stationary Hospital, C.E.F.) were present at the annual dinner of the Unit, at Halifax, on December 7th. Colonel John Stewart presided, and among those who made addresses were Colonel E. V. Hogan and Captain John Rankine.

As part of a drastic endeavour to effect economies, the managing board of the Highland View Hospital, Amherst, have dispensed with the services of two graduate and five pupil nurses. According to newspaper reports the deposed nurses feel that their summary dismissal without notice is unwarranted, and they may take legal action against the hospital board.

The fourth annual meeting of the Western Kings Memorial Hospital Association, held on the sixth of December, was characterized by excellent reports and addresses indicating the pride and interest taken by the people of Berwick and vicinity in the hospital. There has been substantial growth in its work, and the financial situation is very satisfactory. District nursing is being done by members of the nursing staff of this hospital.

In a paper contributed to the December number of Health Rays, an excellent monthly magazine published by the patients of the Nova Scotia Sanatorium, Dr. A. F. Miller pleads for more generous co-operation of the municipal authorities with the provincial government in making proper treatment more readily available to needy persons suffering from tuberculosis. While the tuberculosis death rate of Nova Scotia has been materially reduced within recent years, it is still distressingly high, and Dr. Miller continues tirelessly in the endeavour to bring about further betterment.

Dr. J. G. MacDougall and Dr. R. A. H. MacKeen have been elected President and Secretary, respectively, of the Halifax Branch of the McGill Graduates Society.

W. H. HATTIE

## NEW BRUNSWICK

The scarlet fever situation is again causing distress, especially in Albert County, where for some time sporadic cases have kept the public health authorities extremely busy. Dr. C. A. King, Medical Inspector of Schools, has this area under his supervision and hopes that the situation is now under control. Scarlet fever has for the last twelve months been a serious problem throughout rural New Brunswick.

At the meeting of the York County Council, held in Fredericton on January 8th, Dr. B. W. Robertson brought up the question of the lack of physicians in rural portions of the province. Dr. Robertson stated that there were now in this county only six doctors, as compared with fifteen when he started practice twenty-three years ago. He felt that the only solution for this under staffing of the country physicians lay in some form of state medicine. This matter was given extensive publicity in the papers at the time and has aroused an unusual amount of comment.

The increasing use of the automobile and the conditions of the roads has been a cause of several accidents to physicians this winter. Recently, we reported the death of Dr. Johnson, of Vancebro, when his sedan was struck by a train on December 15th.

Dr. J. F. L. Brown of Woodstock was injured in a similar accident when his car was struck by a Canadian National freight train. Dr. Brown was severely shaken up and received some bad lacerations about the head and body.

Still more recently, Dr. A. E. Macaulay, Saint John, was the victim of an accident in which his automobile and a tram car were involved.

The latest Extra-Mural Tour of New Brunswick has just been completed. The speakers were: Dr. Norman Gwyn, of Toronto, and Dr. Ralph Powell, of the Montreal General Hospital. Dr. Gwyn spoke on "The pathology of rheumatism" and some new features in "The treatment of anæmia." Dr. Powell spoke on "Traumatic injuries to the genito-urinary tract, with special reference to automobile accidents." Both speakers were fortunate in delivering addresses of more than usual appeal to the profession. They spoke in Fredericton, St. Stephen, Saint John and Moncton. The meeting at St. Stephen was the first extra-mural one held at this point and turned out to be an absolute success. Dr. Gwyn was kind enough to address the luncheon members at Saint John on some aspects of the early life of Osler. This was an unexpected treat, and Dr. Gwyn's researches into Osler's life discovered many unusual points of interest in the life of this great man.

A STANLEY KIRKLAND

## QUEBEC

High figures of infantile mortality are revealed in the September report of the vital statistics branch of the Provincial Health Department.

Rimouski, with a rate of 454.5, leads the way, there being five deaths of children under one year of age, out of a total of 11 births there during the month. Montmagny had a rate of 428.5 for the month, there being three deaths out of a total of seven births, while Trois Rivières, with a rate of 304.4, was third, recording 32 deaths of children under one year of age out of a total of 94 births. Another city which recorded an exceptionally high figure was Granby, which registered 333.3 in the infantile mortality column, with 8 deaths out of 24 births.

Only three cities and towns recorded a clean sheet for the month, these being Outremont, Rivière du Loup and Victoriaville, while six other places registered one fatality during the month, these being Grand'Mère, Westmount, St. Jean, Valleyfield, Jonquières and Kenogami.

The general provincial infantile mortality rate for the month was 149.6, consisting of 893 deaths out of a total of 5,969 births, and the urban centres again were over the average, their figure being 491 deaths for a rate of 178.6, as against 402 deaths in the rural area, for a rating of 155.9.

Cap de la Madeleine led the province in the birth column, with a rate of 84.2 per thousand, followed by Thetford Mines, with 53.1 per thousand, and Jonquieres, with 50.7 per thousand.

Causes of death tabulated during the month of September showed that there were 133 violent deaths, the list further including: whooping cough, 27; diphtheria, 23; measles, 1; scarlet fever, 6; typhoid fever, 21; influenza, 24; pneumonia, 127; pulmonary tuberculosis, 163; other forms of tuberculosis, 52; infantile paralysis, 5; spinal meningitis, 15; diarrhœa, 357; encephalitis, 2; syphilis, 6; diabetes, 21; heart disease, 200; and cancer, 149.

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The Executive Committee of the Montreal City Council has ratified the names of those nominated to constitute the new Board of Health Survey more than a year ago and also advocated by Dr. S. Boucher, medical health officer, in his report on the ways of combating tuberculosis and protecting public health.

The board is authorized under a by-law adopted both by the Executive and the City Council, and consists of nine members as follows:

Ald. A. A. DesRoches, representing the Executive, who will be chairman; Dr. S. Boucher, medical health officer; two members from McGill University, Dr. A. Grant Fleming, director of public health, and Dr. F. Pedley; two from the University of Montreal, Dr. L. de L. Harwood, dean of the medical faculty, and Dr. E. G. Asselin; and three members from the City Council, all doctors, Aldermen Quintal, Tessier and Z. Lesage.

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Now that the Provincial Government has agreed to pay 60 per cent of the cost of the building of the new sanatorium projected by the Bruchesi Institute, and the city has already offered to pay the other 40 per cent, the plans are being matured.

A delegation, composed of Louis Lymburner, Dr. J. A. Jarry, Theo. Trudeau, and M. Massicotte, which visited Hon. Athanase David, Provincial Secretary, accompanied by Hon. J. L. Perron, have obtained the assurance that the Government would contribute $960,000 to the project, while the City of Montreal has already promised to furnish the remainder of the $1,600,000 necessary for its construction.

Camp David, at St. Hypolite, will be enlarged so as to be in a position to receive 250 boys, in addition to the 250 girls already under its care. Plans for the enlargement, prepared by Irenée Vautrin, have been accepted, and it is expected that the new building will be ready to receive its additional patients in the early spring.

The enlargement of Camp David has been rendered possible by the donation of an adjoining property, bought by Mr. Perron, at the cost of $10,000.

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The Junior Red Cross in the Province of Quebec is an organization of children, now consisting of more than one thousand groups and of more than thirty thousand members in the Province of Quebec, which is doing work in the interest of better health that deserves every possible support.

Very wisely, the adults responsible for launching the work have left its actual carrying out to the children themselves. Organized in the schools, the teachers refrain from interference or even from giving advice, unless they are asked to do so. The object of the organization is the enforcement of cleanliness, the maintenance of simple sanitary rules and the inculcation of the spirit of service to humanity. The children themselves, through an organization of their own service to those among them who need assistance. The Junior Red Cross, of which A. E. Holt is chairman, is of course affiliated with the Canadian Red Cross Society.

The rapid and apparently permanent growth of the movement among the school children of Quebec is most encouraging not only for the immediate effect which it must have upon the children of to-day, but for the wider and more lasting results that will follow when the children of to-day become the adults of to-morrow.

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Dr. J. P. Decarie of the Provincial Health Department, states that the experiment of removing from homes infected with tuberculosis children not yet affected by the disease and bringing them to more healthful surroundings in the country, which was started last year, will be continued and extended this year. It is realized that, properly managed, the new health service may help to strike at the very root of the evil.

Already little children, from a few weeks old to six or seven years, have been removed to St. Hypolite in the Laurentians, in the neighbourhood of the David Preventive Camp, and placed with highly-recommended families, there to be brought up and educated under the control of the parish priest. Both the families and the priest receive a monthly allocation from the Government for this service. From now on the experiment will be extended with the greatest care, and it is hoped to obtain by it the same success as that which crowned the efforts of Dr. Granger in France.

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The 38th annual meeting of the Montreal Foundling and Baby Hospital was held on January 20th, Dr. A. D. Blackader in the Chair.

The secretary's annual report, read by Mrs. P. Mackenzie, was in part as follows:—

"The Montreal Foundling and Baby Hospital has now completed its 38th year, which has been a most successful one. During the year there has been a high standard maintained among the babies, no serious epidemics have broken out to hold back the work of the hospital, and the doors have remained open throughout the year. Twenty-nine healthy children have been found excellent permanent homes through adoption.

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"At our last annual meeting we appealed to the public for assistance to meet our pressing debts and steadily growing deficit. Through the interest and generosity of Lord Atholstan, *The Montreal Daily Star* opened a fund for our hospital which raised the sum of $12,567.25 of which *The Montreal Daily Star* itself subscribed $1,000.00. This enabled the hospital to carry on its work for the babies unhampered by the constant struggle with financies.

"Several improvements have been made to the equipment, amongst which are three electric refrigerators, and a new sterilizer. The milk-room has been remodelled to suit our present needs, and new flooring has been laid on the ground-floor corridors."

The report of the treasurer, read by Mrs. J. C. Cameron, for the year ending December 31, 1929, showed that the ordinary revenue was $24,403.48; the ordinary expenditure, $32,588.72 and the excess of expenditure over revenue, $8,185.24. "This deficit," the report states, "was wiped out by the amount raised by the *Montreal Star's* appeal to the public and a legacy received by the hospital which left a credit balance of $5,813.58 to transfer to the capital account."

The need for increased accommodation in order to carry on the work adequately was stressed.

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An architect is to be chosen for a hospital in Montreal to be situated at the corner of Cote des Neiges and St. Catherine Road. The Jewish Hospital Board are the owners and it is understood that the purchase of a site is to be completed with all possible dispatch. The cost is $1,000,000.

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At the annual meeting of the Action Médicale, held in the Cercle Universitaire last December, Dr. J. E. Desroches, director of the College of Physicians and Surgeons of the Province of Quebec was elected president for the coming year. Dr. P. Del Vecchio was chosen first vice-president; Dr. J. P. Lafrenière, second vice-president, and Drs. R. Bourgon, W. Descoteaux, F. L. Demers, L. A. Hebert and J. A. Manseau were elected directors. Dr. J. E. Laberge was chosen secretary-treasurer.

The Action Médicale is a professional organization which has existed for many years, principally among French-speaking medical men, for the purposes of mutual help in the advancement of medical science, the improvement of medical technique and the maintenance of professional ethics.

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A farewell dinner was tendered Col. J. T. Clarke, Canadian Army Medical Corps, when about 70 of his old comrades met on December 14th last at the Mount Royal Hotel, Montreal. Colonel Clarke is leaving Montreal to go to Ottawa as Director-General of Medical Services, Canada. All present were returned C.A.M.C. men, residents of Montreal, and this was their first official meeting since the war.

Recalling incidents that occurred overseas, Colonel Bazin, D.S.O., proposed a toast to the C.A.M.C. He remarked that while he had made many friends both before and after the war, those formed during those terrible four years were the only real comradeship he had ever known. The toast was answered by Brig-Gen. Birkett, who gave a history of the corps, and spoke of events during the forty-three years he had been connected with it. A presentation of a silver salver was made to Mrs. Clarke, and acknowledged by the Colonel in her absence.

Col. Cameron, Col. Archibald and Major Hurtubise spoke about the corps, and mentioned incidents recalled by the decorative escutcheons and flags of the different units on the wall of the dining-room. It was agreed that the dinner had been such a success that it should be an annual event.

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A legacy of $10,000 has been left the Montreal General Hospital by the late Robertson Macculloch.

## MANITOBA

At the regular annual meeting of the honorary staff of the Winnipeg General Hospital, Dr. W. Harvey Smith, who recently tendered his resignation after thirty four years of service on the staff, was presented with a piece of plate suitably engraved. Dr. Smith, however, has been appointed consultant, and in the election of officers he was unanimously re-appointed Chairman of the staff, and Dr. R. D. Fletcher was re-appointed Secretary. Dr. Fred Hart was elected a member of the Training School Committee. Dr. Geo. F. Stephens, Superintendent of the hospital, was congratulated on showing a profit on operation of $7.74, with a maintenance expenditure (including financial charges) of $796,625.54.

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The Winnipeg General Hospital has recently installed an automatic sprinkler system covering the basement section, at the cost of $6,000, and equipped the older parts of the building with tubular fire escapes at the cost of $5,000.

Early in January Winnipeg physicians were privileged to welcome Sir Charles Ballance, the distinguished London surgeon, who is returning home after almost a year spent in Egypt, Australia, and various points in North America. While in Winnipeg he was the guest of Dr. S. W. Prowse, Dean of the Faculty of Medicine. On December 31st, Sir Charles was the guest of honour at a luncheon under the auspices of the Winnipeg Medical Society. On January 2nd he addressed the Eye, Ear, Nose and Throat Section of the Winnipeg Medical Society on "The history of the mastoid operation," and on January 3rd he addressed the Winnipeg Medical Society on "Nerve anastomosis with especial reference to the facial nerve." The latter address was illustrated with numerous lantern slides. Though the distinguished lecturer referred to such giants of bygone days as Virchow, Pasteur, and Sir James Paget, who had been his teachers, his address showed that his mind still looks to the future rather than the past.

ROSS MITCHELL

## SASKATCHEWAN

Resolutions from various organizations regarding mental hygiene in Saskatchewan have been forwarded to the government during the past few years.

The Saskatchewan branch of the Social Service Council of Canada asked for psychopathic wards in general hospitals; the Saskatchewan Medical Association asked that feeble-minded children be cared for in some place other than in the mental hospitals; the Provincial Council of Women asked that a commission be appointed to make a mental survey of the province, and that delinquent girls be given a mental examination.

A year ago the late Liberal government in conjunction with the Canadian National Committee for Mental Hygiene appointed Prof. F. R. Laycock as Professor of Educational Psychology at the University

of Saskatchewan, where be began research among school children.

In December, 1929, Hon. F. D. Monroe, Minister of Health, appointed a mental survey commission for Saskatchewan consisting of Dr. C. M. Hincks, medical director of the Canadian National Committee for Mental Hygiene, Toronto; Dr. F. R. Laycock, University of Saskatchewan; Dr. D. E. Rothwell, Regina, Vice-President of the Saskatchewan Medical Council, who has been jail physician in Regina for eighteen years, during which time he has had occasion to examine many mental cases. LILLIAN A. CHASE

## UNITED STATES

The fourteenth Annual Clinical Session of the American College of Physicians will be held at Minneapolis, Minn., from February 10th to 14th.

The officers for 1929-1930 are: *President*, John H. Musser, New Orleans, La.; *President-Elect*, Sydney R. Miller, Baltimore, Md.; *First Vice-President*, Aldred Scott Warthin, Ann Arbor, Mich.; *Second Vice-President*, F. M. Pottenger, Monrovia, Calif,; *Third Vice-President*, Logan Clendening, Kansas City, Mo.; *Treasurer*, Clement R. Jones, Pittsburgh, Pa.; *Secretary-General*, George Morris Piersol, Philadelphia, Pa.

The Executive Secretary is Dr. E. R. Loveland, 133 South Thirty-sixth St., Philadelphia, Pa.

The General Headquarters for the Session will be the Minneapolis Auditorium, and the Curtis Hotel will be the headquarters' hotel. Applications for accommodation may be sent to any hotel the visitor elects, or may be directed to Dr. Norman M. Smith, Chairman, Committee on Hotels, Vendome Hotel, Minneapolis.

Reduced railway fares to Minneapolis have been arranged with railways in Canada and the United States on the certificate plan of one fare and a half. The return journey must be made by the same route as the going journey.

An excellent program has been provided, and there will be symposia on the "Biology of cancer," and on "The rôle of surgery in pulmonary tuberculosis."

### The American Association of Pathologists and Bacteriologists

The annual meeting of the American Association of Pathologists and Bacteriologists will be held in New York City, Thursday and Friday, April 17 and 18, 1930. In order that programs may reach the members in suitable time, contributions should reach the Secretary not later than Friday, March 21, 1930.

One half-day will be devoted to a consideration of Diseases of the Thyroid Gland. One half-day will be devoted to a joint meeting of the American Association of Immunologists. It is requested that contributions to the symposium on Diseases of the Thyroid Gland and to the joint meeting on Immunology be sent in as early as possible.

It is hoped to make the general program comprehensive and consideration will be given to studies in the field of pathological anatomy, histology and physiology, legal medicine, bacteriology, parasitology and immunology.

If contributors wish to make exhibits of materials or methods, dealing with the subject of their papers, they are cordially invited to do so through the American and Canadian Section of the International Association of Medical Museums and are requested to notify as soon as possible Dr. Maude E. Abbott, McGill University, Montreal, Canada. The exhibition rooms will be in close proximity to the meeting rooms. Dr. Abbott will give full directions as to shipments.

HOWARD T. KARSNER, *Secretary*,
2085 Adelbert Road, Cleveland, Ohio.

### The International Association of Medical Museums

The twenty-third meeting of the American and Canadian Section of this Association will be held in the Department of Pathology, Columbia University, 630 West 168th Street, New York, on Wednesday, April 16th, next, being the day preceding the meeting of the American Association of Pathologists and Bacteriologists. The usual program will be presented, consisting of communications, on museum technique and arrangement, microscopic and photographic technique and objective teaching methods, also demonstration exhibits of morbid anatomy, cardiac anomalies and other antenatal pathology and objective results of medical research. Contributions are requested, and titles should reach the Secretary *not later than March 10th*, in order that the programs may be distributed with those of the American Association of Pathologists and Bacteriologists.

The Annual Exhibition of this Association will be held in a room adjacent to the meetings, and will remain open from April 16th to 18th inclusive, for the benefit of members of all the Societies meeting conjointly, who are invited to place material illustrating their papers on exhibition under the auspices of the Museums Association. Material may be forwarded by express, charges prepaid, to *Museums Association, care of Dr. Alvin Pappenheimer, Department of Pathology, 630 West 168th Street, New York, N.Y.*

The headquarters will be at the Hotel Pennsylvania, New York, MAUDE E. ABBOTT, M.D., *Secretary*,
McGill University, Montreal.

### Birth Control

A national campaign by birth control advocates was launched recently with a conference at Columbus, Ohio. The campaign has for its object the repeal of Federal legislation which now prohibits the use of the mails for any matter giving information on contraception or for the transport of contraceptive materials. The plan is to organize the country in four divisions carrying birth control propaganda into every State. The moving spirit of the conference was Mrs. Margaret Sangar who advocated control of conception under the following conditions: (1) to prevent the transmission of diseases to the new-born; (2) to prevent the birth of mentally deficient children; (3) to prevent illness, disability, and death among women who are physically unfit to bear children; (4) to prevent childbirth in adolescence; (5) to enable couples to regulate the size of their families in accordance with their economic means; and (6) to prevent births during the first two years of married life. The last recommendation is supposed to make it easier for married couples to make the psychological adjustments necessary in marriage. It must not be supposed that it would receive the approval of all supporters of the movement. Indeed, in the conference itself there were obvious disagreements about the purposes and consequences of birth control. One speaker regarded it as a cure for overcrowding and a prevention against war. Mrs. Sangar herself now takes the view, so strongly supported by Pearl's studies of population growth, that birth control does not mean limitation but selection of the population.

XUM

### Fatal Automobile Accidents

Early estimates of the total of deaths from automobile accidents during 1929 by the American Automobile Association reach the appalling figure of 27,000 deaths. This is greatly in excess of last year's mortality from the same cause. For the 52-week period ending November 2nd the city death-rate is 25·6 per 100,000, compared with a rate of 22.1 per 100,000 a year ago. Camden, N.J., leads with a rate of 74 and Kansas City is at the bottom of the list with a rate of 10. The main cause of the increasing death-rate is probably the increasing congestion of traffic. The Automobile Association estimates that 2½ million cars will be added to the traffic during this year and make a total of approximately 27 million cars on the roads.

### The New York State Psychiatric Institute

The New York State Psychiatric Institute and Hospital, a unit of the Medical Centre at Broadway and 168th Street, New York City, was formally dedicated and opened to the public on December 3, 1929.

The building is eleven storeys high, cost $2,000,000, and is one of the best of its kind for the study and treatment of mental disease.

### Dr. Ephraim McDowell

The Medical Society of Virginia has erected a bronze tablet to the memory of Dr. Ephraim McDowell, "The Father of Abdominal Surgery," at a point about eight miles from Lexington where he was born.

## GENERAL

### Rebuilding of Paris Faculty of Medicine

The Rockefeller Foundation has offered £1,200,000 towards rebuilding the medical school of the University of Paris. This school was built in 1877 to accommodate 1,000 students, but now holds 5,000. It is well known that the Faculty of Medicine, if rich in professors, has a dwelling only worth what the stones would fetch if it were knocked down. Many attempts have been made by Prof. Roger, dean since the war, to stir up the public authorities, and obtain the necessary money. But hitherto no success has been attained; the money did not seem ready to come. Now the Rockefeller Committee offers $6,000,000 for the purpose, but only under certain conditions. Thus the new Faculty must be a whole block and must be built on a site near the present one and the Latin quarter. Such a site exists, but is at present occupied by the wholesale wine market. This, however, could be moved. The French Government will have to give an equal sum before the Rockefeller grant is made, but the general feeling of the press is that this should be done so as not to miss the chance of making the Paris Faculty the finest in the world.

### A Serviceable Libel

A week or two ago the Paris correspondent of *The Lancet* told how a physician of good repute had exposed a "specific" against tuberculosis composed of cigarette paper soaked and crumbled, and had called the inventor of this priceless remedy a thief and a quack. For this language Dr. Nast was sued for libel, although it was anticipated that, even if he was convicted, the court would let him off lightly. This has proved to be the case, for the sentence passed on Dr. Nast carries the minimal penalty allowed by law—namely, 1 franc of damages to the inventor of the "specific" and a fine of 25 francs, which need only be paid if the malefactor is again convicted within the next five years. It is customary in France for one who is convicted of libel to be ordered to insert an apology in specified newspapers at his own expense, which may be considerable. Dr. Nast has not been required to make any such insertions. The action of the court is regarded as of real significance in medical circles, for, generally speaking, French judges are not specially indulgent to medical men, and have sometimes been regarded as giving them more than their deserts. Dr. Nast, it is clear, is regarded as having done public service in exposing a remedy which had received extravagant prominence in the press to such effect that sanatorium practice was endangered and patients seriously upset by the withholding of a remedy from which they had been led to expect so much. There is still a possibility that the inventor himself may get into trouble for having practised medicine without any qualification.

### The Seventh Conference of the International Union Against Tuberculosis

The Executive Committee of the International Union against Tuberculosis announces the following preliminary program for this Conference, which is to be held at Oslo, Norway, from August 13 to 15, 1930, under the auspices of the Norwegian National Association against tuberculosis.

Tuesday, August 12th, formal opening.

Wednesday, August 13th, "Vaccination against tuberculosis by means of B.C.G.," Prof. A. Calmette, Paris.

Thursday, August 14th, "Thoracoplasty in the treatment of pulmonary tuberculosis," Prof. Bull, Oslo.

Friday, August 15th, "The teaching of tuberculosis to undergraduates, and post-graduate courses on tuberculosis," Professor His, Berlin.

The Conference will be under the august patronage of Their Majesties the King and Queen of Norway.

The Organizing Committee of the Conference has succeeded in obtaining from the Norwegian shipping companies a 25 per cent reduction in the cost of the sea passage as far as Norway, as well as a 25 per cent reduction in the railway fare between Oslo and the frontier. Excursions, at special rates, will also be organized to the principal tuberculosis institutions of Norway.

The Organizing Committee of the Conference would be glad to receive the names of all persons wishing to attend the VIIth Conference of the International Union against Tuberculosis not later than May 15, 1930.

Councillors and Ordinary Members of the Union are invited to the Conference and will receive a presentation copy of the reports and proceedings; they are requested to forward their acceptances either through their government or national association, or directly to the Organizing Committee at the following address:

Cort Adlersgate 6, Oslo (Norway).

Names may also be sent to the headquarters of the Secretariat of the International Union against Tuberculosis at:

2, Avenue Vélasquez, Paris 8e.

No entrance fee will be paid by Councillors or Ordinary Members.

Persons other than Councillors and Ordinary Members of the Union desirous of entering their names as "Members of the Conference" may do so on payment of 25 Norwegian crowns; applications should be forwarded exclusively through their government if the latter represents their country in the Union, or through

*On page 175*
of this issue appears
an article pertaining to
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***CLINICAL DATA***
concerning the treatment of
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their national Association against Tuberculosis if the latter is a member of the Union. Applications sent through other channels cannot be accepted. Payment of the entrance fee should be made by cheque on an Oslo bank to the order of "Tuberculose Konferancen 1930," or by international money-order, preferably in Norwegian crowns or in dollars.

Members of the family of persons attending the Conference will be entitled to the same privileges accorded to delegates whose names have been duly registered, on payment of a reduced contribution of 15 Norwegian crowns. This contribution, however, does not entitle them to receive the official proceedings of the Conference.

Ten speakers, representing ten different countries, have been designated by the Executive Committee to open the discussion on the three scientific questions at the morning sessions. Delegates wishing to take part in the discussion at the afternoon meetings may enter their names beforehand at the headquarters of the Norwegian Association or of the International Union against Tuberculosis, where applications will be considered in order of priority.

### The Ninth Intensive European Course in Otolaryngology

This course which covers the anatomy, physiology, pathology, diagnosis and surgery will be given by the best teachers in Vienna during the summer of 1930. It lasts for five weeks, averaging ten hours a day. All courses are given in the English language.

### The Ninth Intensive European Course in Ophthalmology

This course is just as comprehensive as the one offered in otolaryngology, and will take place in Vienna at the same time. It covers three hundred hours, and includes operations on pigs' eyes, cadaver work, slit lamp and red free ophthalmoscopy.

For further particulars about any of these courses, address Dr. George W. Mackenzie, 1724 Spruce Street, Philadelphia, Pa.

## Book Reviews

**Tumours Arising from the Blood Vessels of the Brain.** Harvey Cushing and Percival Bailey. 219 pages, 159 illustrations. Price $7.50. Charles C. Thomas, Publisher, Springfield, Ill., 1928.

In their introductory remarks Cushing and Bailey note that twenty years ago the neurologist did well to recognize the presence of a brain tumour and to localize it with sufficient accuracy to enable the surgeon to expose it. They add that to-day we have gone far beyond this stage. It is contributions such as their present one that has made this advance possible.

Since the natural history of the different kinds of brain tumours and their favourite sites of predilection is becoming better understood it is sometimes possible to predict with accuracy the histological type of the tumour before operation. This is not only of prognostic value but of great import to the surgeon who has the responsibility of planning the operative procedure. He can foresee difficulties and calmly guard against them. Sudden emergencies arise then with much less frequency.

In 1926 Cushing and Bailey described the tumours of the glioma group. They gave the end results on this group of tumours covering an experience of twenty years. It is only in clinics arranged as Dr. Cushing's is that such valuable studies are possible; that is, clinics where the full responsibility for clinical diagnoses, operative treatment, pathological report and the close following up of the results of treatment are assumed.

Now, out of their 1,522 verified intracranial neoplasms they report the group of blood vessel tumours under two subdivisions; the angiomatous malformations and the hæmangioblastomas. These tumours represent a scanty 3 per cent of brain tumours. Their detailed clinical histories, surgical treatment, careful histological studies and the final results make the story of this group of neoplasms complete. Again, points are brought forward to make the presumptive diagnosis of this tumour group feasible pre-operatively.

They do not include in this presentation extradural angiomas, those from the diploic sinuses, the midline cavernous hæmangiomas of the scalp which sometimes communicate with the longitudinal sinus, and they touch only in passing the angiomas of the spinal cord and those of the envelopes. They have confined themselves entirely to the blood vessel tumours of the brain alone.

The general arrangement of the book and the illustrations are excellent. A summary which is wonderfully complete, though it covers considerably less than two pages, outlines the cardinal facts and is excellent for quick reference. For the neurosurgeon the book is indispensable. For the neurologist it is of much interest not only because it outlines so clearly the clinical earmarks of these tumours, but because it gives in detail the results to be expected when operative interference is advised. W. V. CONE

**A Diabetic Manual.** Elliot P. Joslin, M.D. Fourth edition, 248 pages, illustrated. Lea & Febiger, Philadelphia, 1929.

There may be diabetic manuals which are simpler and more direct but none are more hopeful or more encouraging than this one.

The twenty-seven chapters deal with the recent improvements in diabetic treatment, diabetic arithmetic, hygiene for the diabetic in which the necessity for exercise is stressed, and the diet of diabetic individuals, regarding which he says "it is reassuring to see a diet which contains more grams of carbohydrate than grams of fat," and "I like to see the carbohydrate at least 70 grams and seldom below 100 grams."

Under the heading "Who should use insulin" he says "If a diabetic is not happy, energetic and a joy to himself and to his family, and his urine sugar-free, he had better take insulin." He advises the four times a day urine test for children.

Detailed instructions for care of the feet is given. The chapter on heredity and marriage is concise. Many food tables are given also height and weight tables and expectation of life tables. The illustrations of healthy, happy diabetic children should encourage parent readers.

Those who should buy this book include: diabetic patients; parents of child diabetics; all general practitioners, so that they may know what to expect of the diabetic specialist to whom they refer their diabetic patients; all doctors who are specially interested in the treatment of diabetics, so that the optimism of this book may be transferred to the faithful patients, public health nurses, and social service workers, who round up backsliders and see that they

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LILLIAN A. CHASE

**Hæmodynamics.** P. B. Kittel, F.R.C.S. 195 pages, 3 plates and other illustrations. Price 10/- net. H. K. Lewis Co., London W.C.1, 1929.

This is an extremely interesting and valuable little volume. Interesting, not only to the practising surgeon, but also interesting to the young student in that it is quite original in the explanations of the various phenomena met with in those suffering from varicose veins.

The volume may be divided into two parts. The first and major part has to do more with the scientific investigations and explanations of various phenomena met with. The other deals with treatment, results of the treatment, etc.

In the first part of the volume, there can be only one criticism, and that is the fact that the sentences sometimes are very long and complicated, and the ideas in certain cases are expressed in a laborious way, making it difficult to translate. It demands considerable mental exertion, and consequently is somewhat tiresome to read. In this way it differs somewhat from the writings, we will say, of the late Sir Clifford Allbutt.

The book as a whole is a very valuable one and is written by two men who are quite conservative and very careful workers. It should be read by every one attempting to do anything with varicose veins.

G. R. PETERSON

**The Pathology of the Eye.** Jonas S. Friedenwald, A.M., M.D., F.A.C.S. 332 pages. Illustrated. Price $5.00. Macmillan Co., Toronto, 1929.

This work of 327 pages, beautifully illustrated by Miss Helenor Campbell with 253 microphotographs and drawings, is described by the author as the outcome of his course of lectures to students and surgical house officers in the Department of Ophthalmology at the Johns Hopkins Medical School. It consists of the following chapters: (1) Introduction; (2) Ocular Inflammations; (3) Ocular inflammations (continued); (4) Ocular inflammations (continued); (5) Injuries of the eye; (6) Cataract; (7) Glaucoma, hypotension, detachment of the retina; (8) Senile changes and arterio-sclerosis; (9) Choked disc and albuminuria retinitis; (10) Diseases of metabolism, of nutrition, of the blood, of the endocrine glands, and of the bones; (11) Diseases of the corneal conjunctiva; (12) Diseases of the ocular adnexa; (13) Normal variations, congenital anomalies; (14) Hereditary diseases; (15) Tumours. There are also a useful appendix on microscopical technique and lists of references at the end of most of the chapters.

Throughout the text the author frequently expresses original views obtained from experimental study. The illustrations are especially good, not only in their detail but also in their choice and arrangement. It is a positive delight to be able, on the same page, to compare normal variations, or the normal with the pathological, and such as a hypertrophic ciliary body in hyperopia with an atrophic ciliary body in myopia.

Illustrations in many books by their poor arrangement lose any value which they might have: in this book the illustrations are so arranged that they enhance its value immensely. The publisher, the author, and Miss Helenor Campbell are to be heartily congratulated upon its production. The appearance, the type, and in fact the whole makeup of the book is splendid.

S. HANFORD MCKEE

**Gynecologic Technic.** Thomas H. Cherry, M.D., F.A.C.S. 678 pages, 558 illustrations. Price $8.00. F. A. Davis Co., Philadelphia; Macmillan Co. of Canada, Toronto, 1929.

In the preface the author announces that this is intended primarily as a technical work on gynæcology, especially for the practitioner of medicine who comprehends surgical technique, and who has a special leaning toward gynæcology. This end has been successfully accomplished in Dr. Cherry's book. The subject matter is complete, and is dealt with in the methodical manner of a teacher of experience. The technique of carrying out gynæcological treatment, both surgical and medical, is at hand with the minimum of reading, and admirably illustrated by line drawings from the author's own pen. Only the procedures found most satisfactory in the writer's hands are described. The work thus escapes being burdened with descriptions of superfluous operations. Details of physiology, symptomatology, and diagnosis are largely omitted.

The first 522 pages are devoted to the surgical aspect of gynæcological practice, and include an excellent anatomical description of the structures concerned in pelvic disease. The standard operative procedures are described step by step.

The radium treatment of uterine cancer is described in some detail. The indications for, and the technique of, spinal anæsthesia are included. This section of the book concludes with an account of the after care of operative patients.

Section 2 is concerned with medical gynæcological technique, and includes a discussion of the treatment of gonnorrhœa with particular reference to diathermy. The use of diathermy, cautery, and electro-coagulation in gynæcology is described in some detail. The cautery and electro-coagulation are urged for pre-cancerous cervical conditions. The technique of some of the newer diagnostic methods, such as the gas inflation test, the compatibility test, and utero-salpingography, is described.

The book closes with a useful résumé of the treatment of gynæcological conditions commonly met with in the office and clinic.

A. M. GOODWIN

**Grenz Ray Therapy.** Gustav Bucky, M.D., and Walter J. Highman, M.D. 170 pages, charts. Price $3.85. Macmillan Co., Toronto, 1929.

This book begins with a definition of Grenz rays as soft roentgen rays having wave lengths of from one to three Angstrom units which are produced in lithium glass x-ray tubes with voltages of from four to ten kilowatts.

The physics of the rays is fully discussed, with considerable attention to dose measurements as well as description of apparatus, tubes, the spectrum of Grenz rays and skin absorption, by Otto Glasser, of the Cleveland Clinic Foundation. This portion of the text is highly technical and may be with difficulty grasped by the practising roentgenologist. Another collaborator, Dr. Olga Becker Manheimer, elaborates the theory of the Leucocyte Sturz and advocates the adoption of the word into English as any translation is clumsy.

The author describes technique and application of this form of therapy. He provides the results of experimental work on animals, followed by case histories of clinical cases. The indication for the use of this agent is divided into (1) skin diseases, (2) diseases of internal organs. Criticism of Grenz rays is refuted, and the danger of sequelæ is denied, provided that ordinary care and skill are exercised.

A useful bibliography is supplied. The book is not easily read, as it presents the studies of Dr. Bucky more from the viewpoint of the physicist than of the clinician.

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**Recent Advances in Pulmonary Tuberculosis.** L. S. T. Burrell. The Macmillan Company of Canada Ltd., 1929. Price $3.75.

Most of this book deals with the treatment of tuberculosis, and is intended for the use of practitioners and medical students.

Properly, I think, almost half the book is devoted to pneumothorax and other methods of collapse treatment. The author has had extensive experience with pneumothorax treatment and deals with this subject very well. It is doubtful whether this form of treatment ought to become frequent among general practitioners; the first stages should be done in an institution by a person who has had some training in its performance.

Of the other forms of therapy the use of "sanocrysin" and the "shock treatment" are the two which appear to be recent. The author thinks that the former has its place in the treatment of certain types of tuberculosis and mentions striking results from the latter. It is strange that the use of sanocrysin has not gained any popularity on this side of the Atlantic. Rest is still the mainstay in the treatment of tuberculosis and no striking advance, apart from collapse therapy, has been made in recent years.

The chapter on diagnosis might well have been written fifteen years ago, as there is nothing new presented in it, with the exception that it points out the necessity of differentiating between clinical pulmonary tuberculosis and latent infection. There is an excellent chapter on radiology and some beautiful reproduction of x-ray films.

Mention is made of the Grancher system and of the use of B.C.G. With regard to B.C.G. the author believes that some immunity is produced which lasts for an unknown length of time, and he doubts the likelihood of the bacillus regaining its virulence.

D. L. MENDEL

**Diseases of the Stomach.** Max Einhorn, M.D., Emeritus Professor of Medicine at the New York Post-Graduate Medical School and Hospital. Seventh Revised Edition. New York, William Wood & Co., 1929. Price $6.00.

The seventh revised edition of this well known text-book maintains the high standard set by the previous editions. The many advances which have been made in gastro-enterology since the first edition (1896) have necessitated the rewriting of certain sections. The descriptions of the various methods of examination, many of which have been devised by the author, are detailed and complete.

In the preface to this edition the author has mentioned the present day tendency to neglect the functional and nervous affections of the stomach, and emphasize only the demonstrable pathological lesions. In view of this, the chapters on functional and nervous conditions have been retained in full. They are ably presented and will repay careful study.

The format of this edition is exceptionally good and the work undoubtedly deserves continued popularity.

C. J. TIDMARSH

**Text-Book of Embryology.** Frederick Randolph Bailey, A.M., M.D., and Adam Marion Miller, A.M. Fifth Revised Edition. 687 pages, 529 illustrations. Price: $7.00. William Wood & Co., New York, 1929.

This book is pleasantly and lucidly written and contains a great deal of interesting and valuable material. The fact that it has passed through four editions since it made its first appearance in the year 1909, and now enters on a fifth edition, is evidence that it has found a place for itself. According to the preface to the first edition this text-book, as originally planned, is an outgrowth of the course in embryology given at the Medical Department of Columbia University. As the work took form, it seemed best to broaden its scope and make it of greater value to the general student of embryology and allied sciences.

The type has evidently been kept standing for the present edition as the following points will show. On turning to the seventh line on page 334 one will observe that a period (full stop) has been omitted; then on turning to the index, in search of information on decidual cells and on anomalies of the eye, one will find that incorrect references are given. Now, the same period was omitted after the same word, on the same line, on the same page, in the fourth edition. These references, however, were correct for the fourth edition. The only chapter that has been added to is the one on the Nervous System. It has been enlarged by 28 pages, mainly owing to the inclusion of a number of illustrations of developing nerve endings. Accordingly, prior to page 417 the index is equally correct for both fourth and fifth editions; subsequent to page 560 it may be necessary to add 28 to the number quoted in the index, but this is easily done. A number of paragraphs—occasionally whole pages—have been deleted from the fourth edition to be replaced by paragraphs—or pages—of precisely the same number of lines in the present edition. In order to achieve this perfect refitting the student's convenience has been sacrificed to that of the publisher, as for example, on pages 222-227, where half a dozen of the well known diagrams, illustrating the work of McClure and Butler on the development of the abdominal veins, are reproduced at approximately half their original size with a resulting very great loss in clearness.

It is a poor book that has no errors! A few noted in this fifth edition may be pointed out on account of their practical importance. On p. 146 we read, "in the heads of the long bones, in the ribs, and in the short bones the marrow retains its earlier character and is known as "red marrow." But does it remain in the short bones? And, what of the vertebræ, sternum, and skull? On p. 169, speaking of the carpal bones, it says that ossification "begins in the hamate and capitate during the third year, in the others at later periods." But have these bones not been shown to begin to ossify in at least 7 per cent of females, before birth? From p. 333, we gather that the recurrent branch of the laryngeal branch of the vagus nerve passes behind the fourth aortic arch. Is it not around the sixth arch, which on the left side becomes the ligamentum arteriosum? On p. 336 it appears to be implied that the right lung of man has an infra-cardiac lobe lying between the diaphragm and pericardium; but this is not the rule. Of these four instances, perhaps only the last is of especial interest, "to the general student of embryology and allied sciences" mentioned in the preface. But the medical student, the practitioner of the future, should know where blood is formed, should know whether to expect signs of ossification in the carpal bones at birth, and should know the precise course of the recurrent laryngeal nerve which aneurism, tumours, etc., so readily affect. The point is this: is it fair to the medical student, and is it in the best interests of medicine, to enlarge a book and to broaden its scope in order that the diverse requirements of both the general and medical students may be served? Moreover, is it any longer possible for one who is not engaged in the practice of the art of medicine and surgery to undertake the task of writing such a book except in collaboration with, or at least without frequent consultations with, clinicians.

The following instances from several that might be quoted will show that "the intention of emphasizing those features which bear directly upon other branches

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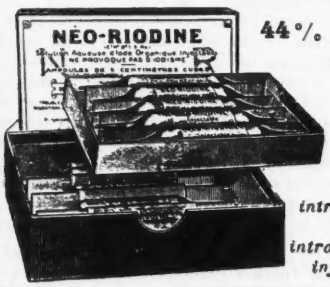


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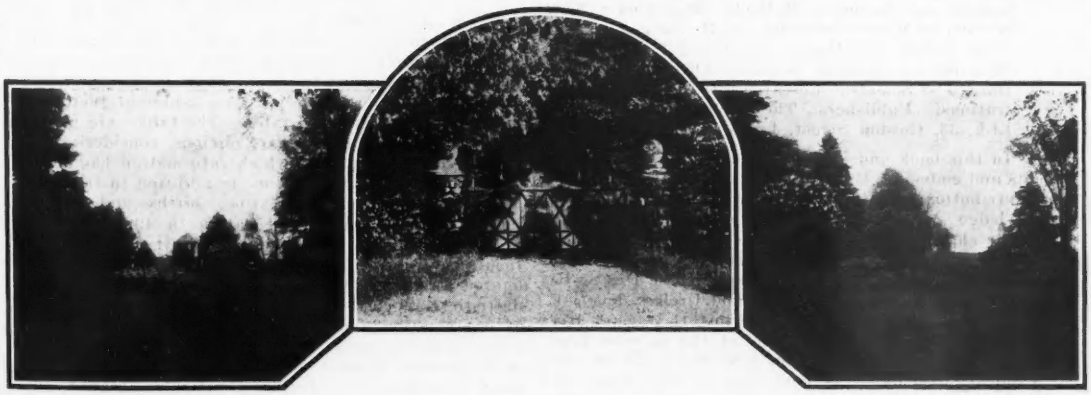

# LOVAT HALL

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XUM

of medicine'' have scarcely been fulfilled. On p. 399 we are advised that the two kidneys may be fused to form the so-called horse-shoe kidney. But, is it not at once embryologically and surgically important to know that the inferior mesenteric artery must arrest the ascent of such a kidney? The surgeon should certainly be led to expect to encounter this artery in front of the organ; one kidney in every 600 is fused. On p. 618, speaking of canalised fibrin, we are told that, ''It is found in relation with the large cell masses among the villi.'' Does it not occur largely on the villi, and why is it called ''canalised''? On p. 608 we are told that by the third month the amnion attaches itself loosely to the overlying chorion, thus obliterating the extra embryonic body cavity. The accoucheur on examining the afterbirth for accessory placentæ reopens this extra embryonic cœlom and therefore requires to know its condition at birth. On p. 203 we are told that the foramen ovale of the heart, ''closes soon after birth,'' and on p. 236, that it closes, ''at birth.'' But is it not patent though functioning in approximately 30 per cent of persons at the age of 15 years?

Though the scope of this book suits the requirements of a particular teacher (or teachers) it is to be remembered that the standard text-books on Anatomy such as Gray, Norris, Cunningham, and Buchanan, one or other of which the student of medicine is expected to posses, contain sections and many references to the subject of embryology.

Seven hundred pages for $7.00! It is at least debatable if the medical student would not receive better value if the book were reduced to half its present size and cost double. For the general and other students it might even be expanded so as to include comparative embryology and experimental embryology.

J. C. B. GRANT

**The Medical Museum. Modern Developments, Organisation and Technical Methods. Based on a New System of Visual Teaching.** S. H. Daukes, O.B.E., M.D., D.P.H., D.T.M.&H., Director of The Wellcome Museum of Medical Science, Affiliated to The Bureau of Scientific Research. 183 pages, 44 illustrations. Publishers: The Wellcome Foundation Ltd., 33, Gordon Street, London, W.C.1, England.

In this book and in the collections which it represents and embodies, the Wellcome Foundation has made a contribution both to medical teaching and to popular knowledge of extraordinary value and of a truly pioneer character. Mr. H. S. Wellcome is to be congratulated on the vision and splendid liberality that have made this achievement possible, and Dr. S. H. Daukes on the organizing genius and tireless devotion to accuracy in detail that underlies the systematic evolution of the various sections of the museum here portrayed. In it we find realized the ideal of the ''Clinical Museum''* as conceived by Sir Jonathan Hutchinson* and other great museum workers of the last century, which is here brought for the first time to adequate and complete fulfilment.

Both the book itself and the system which it expounds are timely, for the conception of the medical museum as a teaching medium of vital importance has become somewhat hazy of recent years. The tendency has been to regard such collections as rather out of date, a relic of the past, and the younger generation has been inclined to look upon them somewhat as a breeder of live-stock might regard a fossil, historically interesting perhaps but an object with which he has no immediate concern. In this book Dr. Daukes has provided a magnificent challenge to all who would question the value of pathological collections. His museum is not a mere assemblage of dry bones or artificially preserved tissues, but a living entity, animated by the ideals and enthusiasm of himself and his colleagues.

One of the most striking features of the museum is the remarkable way in which it is designed by means of extensive labelling and synoptical arrangement to interest and meet the need of all classes of seekers after knowledge. The lay visitor cannot but bring away from its inspection a vivid idea of prevention of disease and of what scientific work may do for the peoples of the earth; the medical undergraduate should find the wherewithal to enlarge his horizon and successfully pass his examinations; special students of any branch will co-ordinate their ideas and find the material here for further research; and curators of museums of all sorts and in all parts of the world will be stimulated to enlarge the scope of their efforts and to feel that they too can make of this their chosen field of endeavour, a living thing.

The value to museum workers of Dr. Daukes' book is further enhanced by the fact that it contains a full discussion of the technical methods used in the Wellcome Museum of Medical Science in the mounting and preservation of specimens, maceration of bone, sealing of jars, methods of display, labelling and classification of material. It is enriched also with a bibliography of recent articles on museum technique, culled largely from the Bulletins of the International Association of Medical Museums, of which the Wellcome Museum has been for many years an active and interested member.

MAUDE E. ABBOTT

**International Health Year-Book.** (Fourth Year, 1928). 1173 pages. League of Nations, Geneva, 1929.

The statistical reports of each country are presented through 28 standard tables, which are considered a minimum to allow for an understanding of health conditions and to permit of comparisons. Seven countries present their reports on tables of their own and not on the standard table. The tables are not all complete for reasons that are obvious, considering the number of sources from which information had to be secured. The standard tables, in addition to the regular tables covering population, births and deaths, include Public Health Legislation in 1927, Hospital Statistics, Sanitary Personnel, and Statistics of Health Insurance Funds. The Canadian section is made up of figures furnished through the Dominion Bureau of Statistics. Special articles of interest are an outline of organization and administration in Australia, and public health progress in Czecho-Slovakia. The reports on campaigns against acute and chronic diseases in many countries are valuable. Particular interest will be directed to the report of the Union of Socialist Soviet Republics. Special reports on Industrial Hygiene in Germany, Belgium and Great Britain form a chapter. There is an outline of the activities of the League of Red Cross Societies and of the organization of the Health Section of the League of Nations. Quite properly, a chapter is devoted to the public health work of the Rockefeller Foundation, whose benefactions are recorded in the reports from many lands. A good index is provided. The volume is a mine of information, presented in a readily usable manner, which will meet with the approval of all those interested in public health. It represents a tremendous amount of patient, painstaking work, for which its compilers are to be highly commended.

A. GRANT FLEMING

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* The Clinical Museum: an Explanatory Address, by Jonathan Hutchison, F.R.C.S., F.R.S., *Brit. M. J.* 2: 1295-1296, 1893.